FAM201A, a Long Noncoding RNA Potentially Associated With Atrial Fibrillation Identified by ceRNA Network Analyses and WGCNA

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Abstract

Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia that contributes to various complications. However, little is known about lncRNAs associated with AF susceptibility. In the present study, we aim to identify lncRNAs involved in pathogenesis of AF based on competing endogenous RNA (ceRNA) network analyses and weighted gene co-expression network analysis (WGCNA).

Methods: Two lncRNA and mRNA microarray datasets GSE41177 and GSE79768 were retrieved from the Gene Expression Omnibus (GEO) database. Differentially expressed lncRNAs (DElncRNAs), mRNAs (DEmRNAs) between AF patients and patients with sinus rhythm (SR) were identified from dataset GSE41177. Then, those DElncRNAs associated target miRNAs were predicted. The ceRNA network was constructed based on DElncRNAs, predicted miRNAs and DEmRNAs. To validate the role of AF-related lncRNAs, all lncRNAs from dataset GSE79768 were selected to perform WGCNA. lncRNA modules relevant to AF were identified. Crucial lncRNAs in the module that was most relevant to AF were screened according to the criteria of |Gene significance (GS)| > 0.6 and |Module membership (MM)| > 0.5.

Results: A total of 18 DElncRNAs and 350 DEmRNAs were identified between AF patients and SR patients. The final ceRNA network contained 5 lncRNAs, 10 miRNAs, and 21 mRNAs. According to the ceRNA theory, combined with the comparative toxicogenomics database (CTD) database, the ceRNA axis FAM201A-miR-33a-3p-RAC3 was considered associated with AF susceptibility. By WGCNA, the blue module was detected most highly relevant with AF. The lncRNA FAM201A was proved in the blue module and highly related to AF.

Conclusions: These results demonstrated that FAM201A might have great potential for susceptibility of AF based on ceRNA network analyses and WGCNA. FAM201A may function, at least partly, as ceRNA to regulate RAC3 in AF susceptibility.

Background

Atrial fibrillation (AF), the most common cardiac arrhythmia, affects approximately 34 million people worldwide, and the number increases with aging[1, 2]. Being a major contributor to stroke, heart failure, sudden death and myocardial infarction, AF poses a significant burden to patients and society[2]. The clinical risk factors of AF include gender, alcohol consumption, smoking, obesity and some clinical comorbidities[3]. Besides, a number of protein-coding genes have been identified significantly associated with risk of AF. Though, only a small proportion of heritability for AF has been uncovered[4, 5]. Until now, the pathogenesis of AF still remains poorly understood, limiting the discovery of novel therapeutic targets for AF.

Long noncoding RNAs (lncRNAs), with more than 200 nucleotides in length, are non-protein-coding RNAs, taking an important part in transcriptional and epigenetic gene regulation[6]. Recently, a large number of studies have demonstrated that lncRNAs involved in pathogenesis of various diseases, such as cancers, diabetes, heart failure and myocardial infarction[7-10]. More importantly, some lncRNAs were proved to

be new biomarkers or therapeutic targets for AF, such as lncRNA HNRNPU-AS1, lncRNA PVT1, lncRNA GAS5[11-13]. Still, little is known about lncRNAs associated with AF susceptibility, which deserves further discoveries.

One pivotal regulatory function of lncRNAs is working as competing endogenous RNA (ceRNA) to regulate mRNA transcription. It was stated in this ceRNA hypothesis that lncRNA could compete for miRNA via shared microRNA response elements, and subsequently sponge miRNA to indirectly regulate mRNA expression[14]. In the pathogenesis of AF, for example, lncRNA PVT1, which was increased in atrial samples of AF patients, acted as sponge for miR-128-3p and up-regulated Sp1 expression to facilitate atrial fibrosis[12]. lncRNA TCONS-00106987 acted as sponge for miR-26 and up-regulate KCNJ2 expression to trigger atrial electrical remodeling[15]. Thus, analyses of ceRNA networks turned to be an efficient method to discover AF-related lncRNAs.

Besides, another biology algorithm, weighted gene co-expression network analysis (WGCNA)[16] can be used to analyze crucial genes or novel biomarkers of various diseases including AF[17]. Briefly, gene modules were constructed and associated with clinical traits to identify disease related modules and the key genes in each module. It is worth noting that not only protein-coding RNAs, but also non-protein-coding RNAs could be used to construct the co-expression networks associated with diseases[18, 19].

For short of AF-related lncRNA microarray datasets, combination of diverse methods or biology algorithms are deeply required to deeply discover lncRNAs involved in pathogenesis of AF. Therefore, in the present study, we aim to identify lncRNAs associated with AF susceptibility based on ceRNA network analyses, as well as WGCNA.

Materials And Methods

Microarray data collection

The lncRNA and mRNA expression profiles of two datasets were retrieved from the Gene Expression Omnibus (GEO) database (<https://www.ncbi.nlm.nih.gov/geo/>). The dataset GSE41177 was used to identify lncRNAs associated with AF susceptibility based on ceRNA network construction, and GSE79768 was used to validate the potential role of lncRNAs for AF based on WGCNA. GSE41177 (platform: GPL570) contains left atrial appendages and paired pulmonary vein and the surrounding left atrial junctions from 3 AF patients and 16 patients with sinus rhythm (SR). GSE79768 (platform: GPL570) contains left atrial appendages and right atrial appendages from 7 AF patients and 6 SR patients. Only data of left atrial appendages in these two datasets were selected for analyses to achieve the sample consistency. Additionally, there are evidences that gene expression files of left atrial and right atrial are not usually identical and left atrial is proved more pivotal in AF initiation and maintenance[20, 21].

Differential lncRNA and mRNA expression analyses

The lncRNA and mRNA expression profiles were retrieved from dataset GSE41177 for differential expression analyses and ceRNA network construction. Identification of differentially expressed lncRNAs (DElncRNAs), mRNAs (DEmRNAs) between AF patients and SR patients were performed using the “limma” package of R software (Version 3.6.3)[23]. The adjusted P value < 0.05 and $|\log_2\text{-fold change (FC)}| > 1$ was taken as the threshold to select DElncRNAs and DEmRNAs. Hierarchical cluster heatmaps were generated to represent expression intensity and direction of DElncRNAs and DEmRNAs using the “pheatmap” package of R software based on Euclidean distance.

Construction of the ceRNA network

DElncRNAs associated target miRNAs were predicted using the miRcode database (<http://www.mircode.org/>), which contains the putative interactions between lncRNAs and miRNAs[24]. Then, these miRNAs associated target mRNAs were predicted based on the miRDB(<http://mirdb.org>), miRTarBase(<http://mirtarbase.mbc.nctu.edu.tw/php/index.php>), and TargetScan(<http://www.targetscan.org>) databases[25-27]. Only those identified in all three databases were selected as target mRNAs. The overlap of target mRNAs and DEmRNAs, together with DElncRNAs and predicted miRNAs, were obtained to construct the final ceRNA network using cytoscape software (Version 3.7.2)[28].

Gene ontology enrichment analyses for mRNAs in the ceRNA network

To reveal the potential biological functions of mRNAs in the ceRNA network, Gene Ontology (GO) enrichment analyses was performed using “clusterProfiler” package of R software[29]. The bar graph was generated to display the enrichment results. The threshold was set as the adjusted P value < 0.05 .

Potential AF susceptibility lncRNAs and mRNAs prediction

The Comparative Toxicogenomics Database (CTD) (<http://ctd.mdibl.org>) database contains data of associations between chemicals, gene products, phenotypes, diseases, and environmental exposures[30]. The CTD database was used to predict the potential AF-related lncRNAs and mRNAs in the ceRNA network, with the inference score reflecting the association between AF and lncRNAs or mRNAs.

Validation for potential role of lncRNAs through WGCNA

The lncRNA expression profiles were retrieved from dataset GSE79768 for WGCNA. All 1210 lncRNAs were selected to construct a co-expression network using the “WGCNA” package in R software[16]. A proper soft threshold of 9 was chosen to satisfy the degree of independence of 0.85 with the minimum value. An adjacency matrix was constructed and converted into a topological overlap matrix to reflect the correlation strength in the co-expression network. Hierarchical clustering was performed using DynamicTreeCut algorithm to construct the network modules with the minimum module size of 30 and height cutoff of 0.25. The module eigengene (ME) is the first principal component of the module,

representing the overall expression profiles of each module. To identify modules relevant to AF susceptibility, the correlation between MEs and atrial rhythm phenotypes were analyzed with Pearson's correlation and visualized by the heatmap. A threshold of $P < 0.05$ was used to screen the modules significantly associated with AF susceptibility. Gene significance (GS) is defined as the correlation between each gene and the clinical trait. Module membership (MM) is defined as the correlation between each gene and each module eigengene. The lncRNAs satisfying the criteria of $|GS| > 0.6$ and $|MM| > 0.5$ were identified as crucial lncRNAs relevant to AF.

Results

Differential expression analyses of lncRNAs and mRNAs in atrial fibrillation

Microarray data of GSE41177 were downloaded and used for analyses. A total of 18 DElncRNAs (Additional file 1) and 350 DEmRNAs (Additional file 2) were identified between AF patients and SR patients, using the threshold of an adjusted P value < 0.05 and $|\log_2 FC| > 1$ as cut-off. The volcano plots showed all RNA expression levels in AF samples compared to SR samples (Additional file 3). The heatmap showed the distinguished expression levels of lncRNAs (Figure 1) and mRNAs (Additional file 4) between AF and SR groups.

Construction of the ceRNA network

We predict the miRNAs that interact with DElncRNAs based on miRcode database. A total of 222 interactions between 6 DElncRNAs and 157miRNAs were identified. Then the target mRNAs of abovementioned 157 miRNAs were predicted based on the miRDB, miRTarBase, and TargetScan databases. Overall, 992 mRNAs identified in all three databases were selected as target mRNAs. The overlap of these 992 mRNAs and 350 DEmRNAs were used to construct the ceRNA network, which finally contained a total of 5 lncRNAs, 10 miRNAs, and 21 mRNAs (Figure 2, Table 1, Table 2, Additional file 5). Except for one up-regulated lncRNA CTD-3080P12, the other four lncRNAs (FAM201A, LINC00326, LINC00029, LINC00355) were all down-regulated in AF patients compared with SR patients.

Table 1 Differentially expressed lncRNAs in the ceRNA network

	logFC	AveExpr	t	P.Value	adj.P.Val	B
FAM201A	-1.17	3.18	-5.97	6.51×10^{-6}	3.58×10^{-3}	3.97
CTD-3080P12	1.09	4.40	5.50	1.89×10^{-5}	5.14×10^{-3}	2.98
LINC00326	-1.86	3.52	-4.69	1.25×10^{-4}	1.14×10^{-2}	1.22
LINC00029	-1.00	5.01	-4.62	1.51×10^{-4}	1.20×10^{-2}	1.05
LINC00355	-1.33	3.42	-3.65	1.51×10^{-3}	3.38×10^{-2}	-1.10

Table 2 Differentially expressed mRNAs in the ceRNA network

	logFC	AveExpr	t	P.Value	adj.P.Val	B
SLC1A5	1.09	6.89	3.30	3.45×10^{-3}	4.89×10^{-2}	-1.86
REST	-1.20	7.10	-5.80	9.58×10^{-6}	4.00×10^{-3}	3.62
PITPNA	1.11	8.21	5.03	5.67×10^{-5}	8.47×10^{-3}	1.96
RAC3	-1.12	5.13	-3.47	2.32×10^{-3}	4.09×10^{-2}	-1.50
FOXQ1	-1.03	4.34	-5.89	7.71×10^{-6}	3.67×10^{-3}	3.82
CSF1R	1.75	9.00	3.66	1.48×10^{-3}	3.35×10^{-2}	-1.08
BOD1	1.99	8.69	3.47	2.29×10^{-3}	4.07×10^{-2}	-1.48
RPA2	2.29	8.54	3.61	1.65×10^{-3}	3.49×10^{-2}	-1.18
DPYSL2	2.37	11.37	3.56	1.85×10^{-3}	3.69×10^{-2}	-1.29
DDIT4	1.09	10.54	4.41	2.50×10^{-4}	1.53×10^{-2}	0.58
KAT7	-1.19	8.58	-4.41	2.45×10^{-4}	1.51×10^{-2}	0.60
TOB1	-1.38	10.11	-3.64	1.55×10^{-3}	3.40×10^{-2}	-1.12
NR3C2	-1.43	8.25	-5.90	7.56×10^{-6}	3.67×10^{-3}	3.84
SEMA4B	-1.05	7.32	-4.35	2.88×10^{-4}	1.63×10^{-2}	0.44
CHL1	-1.07	5.03	-3.42	2.56×10^{-3}	4.32×10^{-2}	-1.59
CRIM1	-1.25	8.94	-4.33	2.96×10^{-4}	1.64×10^{-2}	0.42
TGFBR2	1.20	8.89	3.31	3.32×10^{-3}	4.81×10^{-2}	-1.83
SUCO	-1.46	8.13	-3.73	1.23×10^{-3}	3.12×10^{-2}	-0.91
STAM	-1.07	8.60	-4.48	2.11×10^{-4}	1.42×10^{-2}	0.74
MATR3	-1.40	4.07	-3.35	3.08×10^{-3}	4.68×10^{-2}	-1.76
PTAR1	-1.01	6.88	-3.29	3.52×10^{-3}	4.94×10^{-2}	-1.88

Gene ontology enrichment analyses for mRNAs in the ceRNA network

The results of GO enrichment analyses with the screening criteria of adjusted P value < 0.05 were presented in Additional file 6 and Additional file 7. The mRNAs in the ceRNA network were mainly enriched in transmembrane receptor protein kinase activity, protein phosphatase binding, phosphatase binding, transmembrane receptor protein tyrosine kinase activity. Neither specific function nor specific pathway was identified in the enrichment analyses. The reason for that was speculated to be the small number of mRNAs enrolled in the enrichment analyses.

Potential AF associated lncRNAs and mRNAs prediction in the ceRNA network

LncRNAs are supposed to positively regulate mRNAs by working as miRNA sponges based on ceRNA theory. In our ceRNA network, expression direction of seven down-regulated lncRNA and mRNA pairs were in accord with the ceRNA theory, including two DElncRNAs (FAM201A, LINC00355) and seven DEmRNAs (RAC3, MATR3, NR3C2, KAT7, CHL1, SUCO, STAM). Then, CTD database was used to predict the potential role of above DElncRNAs and DEmRNAs in AF. Inference scores were used to reflect the associations between AF and above RNAs. Finally, one lncRNA and seven mRNAs including FAM201A (Inference score: 3.08), NR3C2 (Inference score: 24.69), RAC3 (Inference score: 22.57), KAT7 (Inference score: 16.61), STAM (Inference score: 9.62), MATR3(Inference score: 5.27), CHL1 (Inference score: 3.77), and SUCO (Inference score: 1.79) turned out to have potential associations with AF. Regarding mRNAs, NR3C2 and RAC3 have relatively higher inference scores for AF. Taking inference scores of both lncRNAs and mRNAs into consideration, the ceRNA axis FAM201A-miR-33a-3p-RAC3 was predicted to have potential role for AF susceptibility.

Validation for potential role of lncRNAs through WGCNA

WGCNA was performed to further validate the potential role of lncRNAs in AF. All 1210 lncRNA expression matrix from GSE7976 were screened for construction of the co-expression network. The sample clustering tree and trait heatmap was illustrated in Figure 3A. The soft-threshold of 9 was set to construct a scale-free network, with the scale-free topology fit index > 0.85 (Figure 3B). The final eight modules identified based on average hierarchical clustering and dynamic tree cutting were shown in Figure 3C.

The module-trait association analysis was performed by calculating the correlation between MEs and the AF phenotype. Blue module ($r = -0.82$; $P = 5 \times 10^{-4}$) and black module ($r = -0.61$; $P = 0.03$) were highly relevant with AF (Figure 4A). The significant correlation was observed between MM and GS for AF in blue module, as shown in Figure 4B. A total of 95 lncRNAs in blue module were identified as crucial lncRNAs associated with AF, according to the criteria of $|GS| > 0.6$ and $|MM| > 0.5$ (Additional file 8). We mainly focused on the MM and GS for AF of lncRNAs, namely, FAM201A, LINC00355, LINC00326, LINC00029, LINC00355, CTD-3080P12, which were identified in the ceRNA network. Finally, FAM201A (GS: -0.62, PGS: 0.02; MM: 0.75, P.MM: 3.35×10^{-3}) and LINC00326 (GS: -0.60, PGS: 0.03; MM: 0.78, P.MM: 1.58×10^{-3}) were in the blue module and proved to be highly related to AF (Table 3).

Table 3 MM and GS for AF of lncRNAs in the ceRNA network

lncRNA	GS	P.GS	MM	P.MM	Module color
FAM201A	-0.62	0.02	0.75	3.35×10^{-3}	blue
LINC00355	-0.20	0.51	0.02	0.96	greenyellow
CTD-3080P12	0.05	0.87	0.25	0.41	pink
LINC00326	-0.60	0.03	0.78	1.58×10^{-3}	blue
LINC00029	0.37	0.21	0.10	0.75	magenta

AF: atrial fibrillation; GS: gene significance; MM: module membership.

Taken together, these results demonstrated that FAM201A might have great potential for susceptibility of AF based on ceRNA network, CTD database and WGCNA. FAM201A may function, at least partly, as ceRNA to regulate RAC3 in AF susceptibility.

Discussion

In the present study, 10 left atrial appendages of AF patients and 22 left atrial appendages of SR patients were enrolled from two datasets, one for screening AF-related lncRNAs by ceRNA network analyses and another for validation by WGCNA. By construction of ceRNA network, combined with CTD database, the ceRNA axis FAM201A-miR-33a-3p-RAC3 was identified associated with AF susceptibility. Subsequently, by WGCNA for lncRNAs, two co-expression lncRNA modules were proved associated with AF and FAM201A was finally validated to be highly negatively related to AF. Collectively, lncRNA FAM201A was speculated to function, at least partly, as ceRNA to regulate RAC3 in AF susceptibility.

FAM201A refers to lncRNA family with sequence similarity 201-member A, located in genomic 9p13.1 with 2.9 Kbp long[31]. FAM201A was demonstrated to be involved in various diseases previously, especially cancers. In patients with lung squamous cell cancer, FAM201A was up-regulated. By regulating ATP-binding cassette transporter E1, FAM201A participated in cell proliferation, migration, invasion and influenced the survival of these patients[32]. In tissues from non-small cell lung cancer patients, elevated expression level of FAM201A was detected related to radioresistance. For these patients, FAM201A-miR-370-EGFR was suggested a key axis in regulation of radiotherapy sensitivity[33]. Another in vivo experiment showed that high level expression of FAM201A involved in development of lung adenocarcinoma and down-regulation of FAM201A exerted the opposite effect[34]. In addition to cancers, down-regulation of FAM201A was reported to be associated with Osteonecrosis of the femoral head through bioinformatics analysis and quantitative real-time polymerase chain reaction experiments[35]. For the first time, FAM201A was revealed to be associated with AF susceptibility in the present study. In order to confirm the potential function of FAM201A on AF, both the ceRNA network analyses and WGCNA were applied. Identical results concerning the function of FAM201A on AF were achieved based on the

two different methods and two different microarray datasets. Thus, these reliable results indicated that down-regulation of FAM201A may serve as potential prediction of AF susceptibility.

The underlying mechanism of FAM201A on AF could be elucidated, at least partly, through ceRNA network analyses. In our constructed ceRNA network, FAM201A regulated RAC3 by sponging miR-33a-3p. Down-regulation of FAM201A and the consequent down-regulation of RAC3 were detected to correlate with AF susceptibility. RAC3 refers to the Rac family of small guanosine triphosphatases[36]. This is the first time that alteration of RAC3 expression from left atrial appendages of AF patients compared with SR patients has been reported. However, expression level of RAC3 was previously reported to be elevated in leukocytes from AF patients compared with controls[37]. Actually, there is a contradiction between their study and the present study. It was believed that the different samples obtained might be responsible for the discrepancy between the findings from this previous study and our study. As stated above, different samples obtained for research could contribute to distinct gene expression[21].

Although RAC3 was not reported directly associated with AF previously, there were indirect evidences that RAC3 could contribute to development of AF. He et al reported that in RAC3 knockdown human umbilical vein endothelial cells, level of autophagy was detected to be much higher, which was related to inhibition of endothelial dysfunction caused by oxidized low-density lipoprotein. The results indicated the role of RAC3 on endothelial dysfunction by down-regulating autophagy[38]. Rubio et al demonstrate that the expression level of RAC3 was negatively associated with autophagy, influencing chemoresistance of colorectal cancer[39]. In a word, RAC3 was verified to have a capacity for down-regulating autophagy. Interestingly, high level of autophagy was observed in both AF patients and rabbit models of atrial rapid pacing[40]. Promotion of autophagy by overexpression of autophagy-related gene7 could lead to decreased L-type calcium channel, diminished L-type calcium current, abbreviated action potential duration, and higher AF incidence. It was also testified that up-regulated autophagy could aggravate the autophagic degradation of L-type calcium channel and the related electrical remodeling in AF[40]. In addition to these findings, the high level of autophagy or autophagy-related gene expression were also observed elsewhere in experimental and clinical AF[41, 42]. Thus, we speculated based on the findings of our study that decreased expression of RAC3 resulting from decreased FAM201A might potentially promote autophagy and the consequent vulnerability to AF. We would indeed elucidate this mechanism in the future experiments.

There were still some limitations in the present study. First, the sample size in our study was not large enough. Although we testified the role of lncRNAs through different methods, more validations were still needed to confirm the role of some key lncRNAs in AF. Second, the expression levels of lncRNAs in the dataset used for WGCNA were relatively much lower than those of protein-coding genes. Much data about lncRNAs identified in the ceRNA network would be missed if we include all protein-coding genes in the analyses. Therefore, in order to obtain as much information about lncRNAs as possible, we performed WGCNA only for lncRNAs, which would inevitably lead to the missing information about lncRNA-mRNA interactions. Third, the GO enrichment analyses failed to provide us significant clues on the underlying mechanisms of AF related to genes identified in the present study, which could be explained by the small

number of mRNAs included in the final ceRNA network used for this enrichment analyses. Thus, the underlying mechanisms related to AF was speculated on previous researches, and further experiments were required to verify this speculation.

Conclusions

In conclusion, we identified an important ceRNA axis FAM201A-miR-33a-3p-RAC3 associated with AF susceptibility through analyses of ceRNA network. The pivotal role of FAM201A on AF was then validated by WGCNA. These findings indicated that decreased expression of FAM201A exerted an important role on AF susceptibility through down-regulating RAC3 and gave us a novel clue on further experiments about the underlying mechanisms of AF.

Abbreviations

AF: Atrial fibrillation; SR: Sinus rhythm; CeRNA: Competing endogenous RNA; WGCNA: Weighted gene co-expression network analysis; GEO: Gene expression omnibus; DElncRNAs: Differentially expressed lncRNAs; DEmRNAs: Differentially expressed mRNAs; GO: Gene ontology; CTD: Comparative toxicogenomics database; LncRNA: Long noncoding RNA; ME: Module eigengene; GS: Gene significance; MM: Module membership; FAM201A: Family with sequence similarity 201-member A; RAC3: Rac family of small guanosine triphosphatases.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the declaration of Helsinki and all methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets (accession number: GSE41177; accession number: GSE79768) used in the present study are available in the GEO database. The dataset GSE41177 can be accessed in the website: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE41177>. The dataset GSE79768 can be accessed in the website: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE79768>.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CX and LY designed the study. CX wrote the manuscript. CX and HXY were responsible for data analyses and visualization. DQ collected and screened the datasets. LY reviewed the manuscript. All authors have read and approved the final manuscript.

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Figures

Figure 1

Heatmap of differentially expressed lncRNAs in AF and SR samples. The vertical axis represents samples, and the horizontal axis represents lncRNAs. Pink color represented AF samples, and blue color represented SR samples. Green color indicates down-regulated expression levels, and red color indicates up-regulated expression levels.

Figure 2

Competing endogenous RNA network of lncRNA-miRNA-mRNA. Diamond represent lncRNAs, triangle represent miRNAs and oval represent mRNAs.

Figure 3

Construction of weighted co-expression network. A. The sample clustering tree and trait heatmap in 13 samples. B. Soft-threshold power analysis. C. Co-expression cluster dendrogram. Each color represents one specific module by WGCNA.

Figure 4

Identification of AF associated module. A. Heatmap of the correlation between the module eigengenes and AF. B. Correlation between MM and GS for AF in blue module.

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