lncRNA-Associated ceRNA Networks in Spleen of Noct1-correlated T-ALL Leukemia Mice

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Abstract

Background

Acute T-lymphocytic leukemia (T-ALL) is a highly aggressive malignant tumor in leukemia. Noth1 is considered as an major oncogene in the development of T-ALL. Increasing evidences have revealed that the occurrence and progression of T-ALL referred to abnormal gene expression, pathway activation and the regulation between these genes. However, the potential lncRNA-associated competing endogenous RNA (ceRNA) network involved in spleen of Noth1-correlated T-ALL leukemia mice remains unclear.

Methods

Overexpression of Notch intracellular domain (ICN) of Notch1 by retroviral infection was used to set up mouse T-ALL model. Deep RNA-sequencing analysis was performed the expression of lncRNAs and mRNA in spleen of T-ALL mice and C57BL/6 mice.

Results

The deep RNA-sequencing analysis shown that 1833 lncRNAs and 4626 mRNAs were deregulated according to the P-value ($p < 0.05$) and fold change (> 2 -fold) in spleen of T-ALL leukemia mice compared with that of C57BL/6 mice. Gene Ontology(GO) and KEGG pathway analysis were performed to reveal the potential roles of differentiated expressed lncRNAs. Co-expression Network was performed to reveal the regulation relationship between the differentiated expressed lncRNAs and mRNAs. CeRNA prediction constructed the lncRNA-miRNA-mRNA model to find the core ceRNA based on regression model analysis and seed sequence matching methods.

Conclusion

This study provided a systematic overview of the altered lncRNAs and mRNA expression, pathway and ceRNA regulation network in the pathogenesis of Noth1-correlated T-ALL.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Tables

Table 1 Basic information of selected nice lncRNAs for qRT-PCR confirmation.

Seqname	Source	RNA length	Locus	P-value	Fold change	Regulation
NONMMUT117521.1	PMID24463510	863	4:137882371-137883938	0.007679055	7.33	DOWN
NONMMUT021309.2	PMID23951020	2508	14:65114738-65117245	0.005231906	5.65	DOWN
ENSMUST00000195494	noncodeV3	2099	2:11532596-11534694	0.000178499	10.60	DOWN
NONMMUT008951.2	noncodeV3	3828	11:24103379-24107440	4.34E-05	12.53	DOWN
NONMMUT008779.2	noncodeV3	3379	11:20461259-20464664	0.00264931	9.67	DOWN
NONMMUT026003.2	noncodeV3	2078	16:23981313-23983390	0.004331438	5.59	DOWN
NONMMUT041921.2	NONCODEv4	3925	2:181405971-181409895	0.000122807	7.66	DOWN
NONMMUT147972.1	-	1666	4:32239436-32241101	0.001742802	8.78	DOWN
NONMMUT029828.2	NONCODEv3	2875	17:46424215-46427089	3.45E-05	32.22	DOWN

Table 2 Specific primers of each lncRNA.

Seqname	Forward	Reverse
NONMMUT117521.1	GATGCTGAGCAAGTGGGTGA	TGGATAGGTGGATGTGAGCG
NONMMUT021309.2	TCCAACATTGCTCACCCGAG	AGCATGGCGCTGTCAATGTA
ENSMUST00000195494	GGATCTGCAGAGGGGCTTAC	GCACCAGGGAACCCATTGTA
NONMMUT008951.2	CAGGACGAGTCAGGCACATT	CAAGCCTTCGGTCTGTGTCT
NONMMUT008779.2	AGTCCTTGTGTGAGCATCCG	CCCATGTGTTCCGTGGAGAA
NONMMUT026003.2	AAGAGGCTGGCTAGACCTGA	AAGGAGTTTGAAGGCGGGAG
NONMMUT041921.2	AAGATGTAAGGGCCACCAGC	TGTGAGGCTGTTCCAAGTCC
NONMMUT147972.1	ACCCAACAAGATGCTCCTCG	AAGTCGCAGTTGGGTCTCTG
NONMMUT029828.2	TTCAGGTTTCAGCTGTTCCGGG	GAGTGGGGAGCCGTAAGAAC

Figures

Figure 1

Differentially expressed lncRNAs and mRNAs in spleen of mice. The time-line of study design

(A). Differentially expressed lncRNAs are shown in volcano Plot(B) 16 and scatter-Plot(C).

Differentially expressed mRNAs are shown in volcano plot(D) and scatter plot(E). For volcano plot, the abscissa is fold change(fold change ≥ 2) and the ordinate is p value(p-value ≤ 0.05). The red color is the up-regulated genes and the blue is the down-regulated genes. For scatter plot, The abscissa and ordinate represent two sets of samples. The red color is the up-regulated genes and the blue is the down-regulated genes.

Figure 2

mRNA GO and KEGG pathway analysis in spleen of mice. TOP10 enriched GO terms for Biological process(A), cellular component(B) and molecular function(C). TOP10 enriched KEGG pathway was shown in corresponded to differentially expressed transcripts(D).

Figure 5

Validation of deep RNA sequence results by qRT-PCR from spleen of T-ALL mice or C57BL/6 mice.

Supplementary Files

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[additional data.xls](#)

[ARRIVE Guidelines Checklist.pdf](#)