Identification of long noncoding RNA RP11-89K21.1 and RP11-357H14.17 as prognostic signature of endometrial carcinoma via integrated bioinformatics analysis

Abstract and Introduction

Endometrial carcinoma is a serious disease as it ranks first in gynecological diseases and second in uterine cancer, so it threatens the life of women.

The earlier it is detected, the better it is to avoid the development and complications of cancer, and to prevent it from spreading to malignant cancer.

Long noncoding RNA (IncRNA) is a noncoding RNA that its length is more than 200pb. IncRNA plays a major role in regulating transcription and translation and is found in physiological and pathological processes and plays a pivotal role in development of malignant tumors.

In this study, we investigated lncRNAs in endometrial carcinoma based on the Cancer Genome Atlas (TCGA) database and identified two lncRNA RP11-89K21.1 and RP11-357H14.17 and connect their role in developing, prognostic value and functional regulatory network of EC. We also found the upstream transcriptional regulatory factors, co-expression genes and binding proteins of lncRNAs and their relationship with immune infiltration. Furthermore, we found their potential roles and molecular mechanisms in EC utilizing competing endogenous RNA (ceRNA) (lncRNA-miRNA-mRNA) hypothesis, which is extremely useful to provide a new strategy for early diagnosis and treatment of EC.

Related Works

circlncRNAnet : it is lack of protein-coding potential, long noncoding RNAs (lncRNAs) and circular RNAs (circRNAs) have explained as key determinants in regulating gene , acting to fine-tune transcriptional and signaling output.

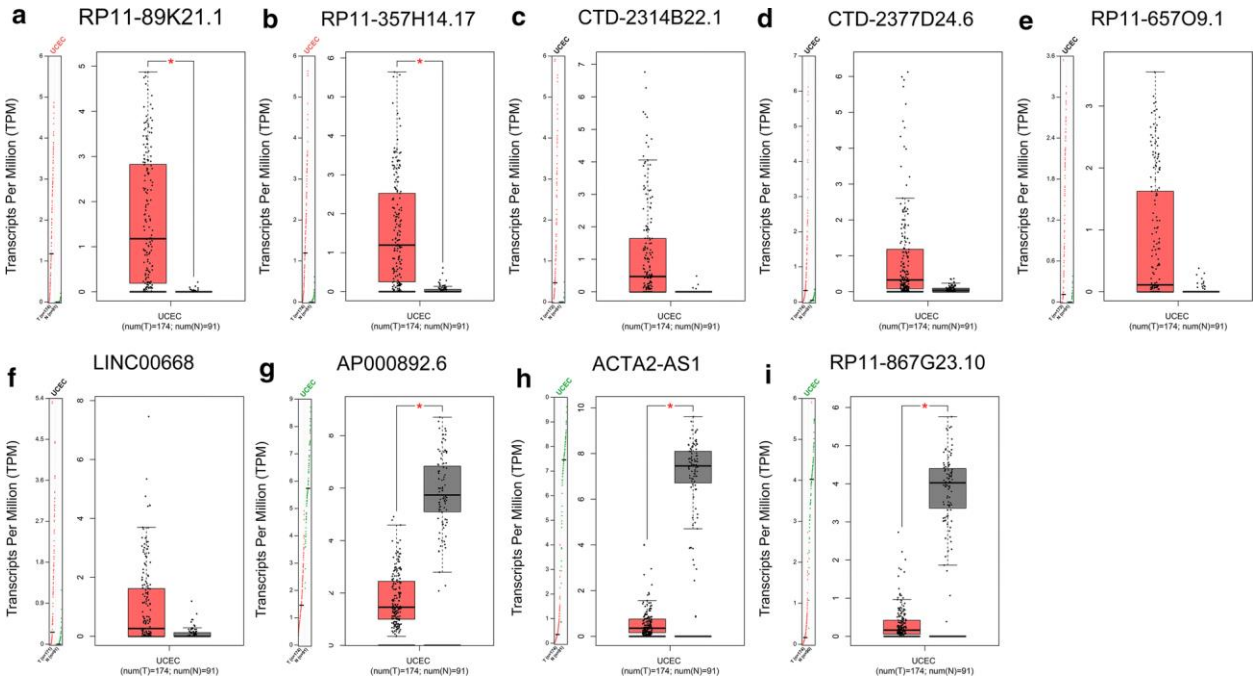
Protein–protein interaction network and transcriptional regulatory network : GeneMANIA is a flexible platform that can expect gene function, analyze gene lists and sequence genes with function assays, that gives three main cases: single gene queries, multiple gene queries and network search. The online tool can construct protein–protein interaction (PPI) network and protein-DNA interaction, investigate potential signal pathway, gene and protein expression and protein domains. We explored lncRNA-related proteins and transcriptional regulatory molecules with AnnoLnc, and visualized the functions and regulatory networks of these molecules using GeneMANIA.

Immlnc :

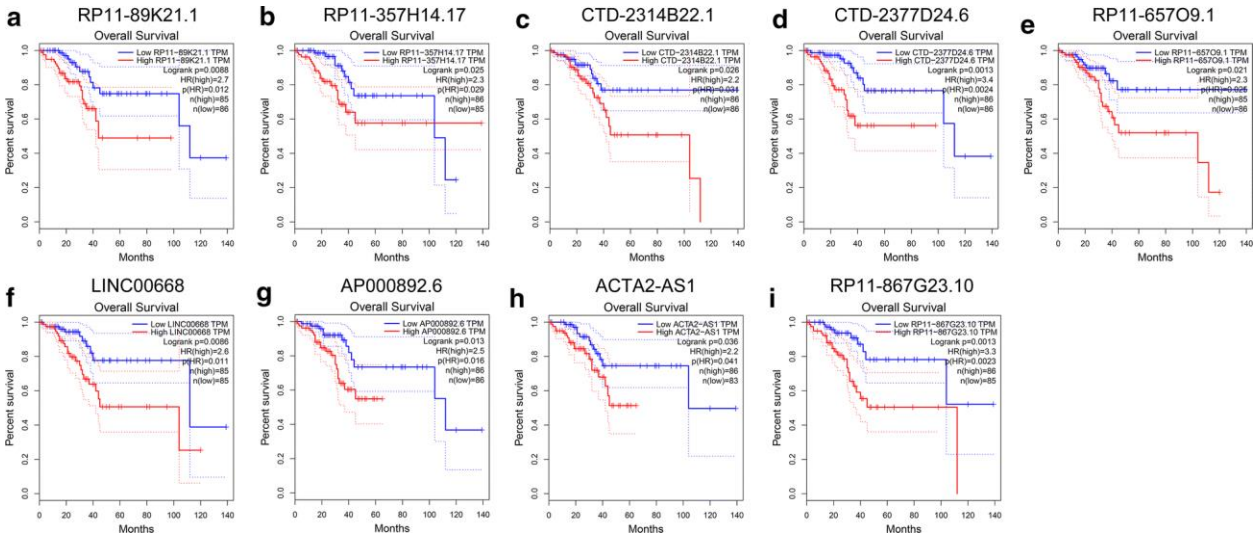
Long noncoding RNAs (lncRNAs) are emerging as critical regulators of gene expression and paly crucial roles in immune regulation. However,high-throughput methods for the identification of

lncRNAs that affect immune pathway activity are still largely unavailable. ImmLnc is a web-based resource for investigating the immune-related function of lncRNAs across cancer types. In this resource, the users can query the lncRNA-pathways, lncRNA-immune cell type's correlation, and cancer-related lncRNAs across 33 cancer types. The ImmLnc pipeline and the resulting data provided here are intended to serve as a valuable resource for understanding the lncRNA function and to further advance the identification of immunotherapy targets.

Results



Expression levels of dysregulated lncRNAs in patients with UCEC validated with GEPIA. **a**, **b** RP11-89K21.1 and RP11-357H14.17 were significantly upregulated validated with GEPIA (both $P < 0.05$). **c–f** The expression levels of CTD-2314B22.1, CTD-2377D24.6, RP11-657O9.1 and LINC00668 in UCEC (all $P > 0.05$). **g–i** AP000892.6, ACTA2-AS1, and RP11-867G23.10 were significantly downregulated in UCEC validated with GEPIA (all $P < 0.05$). TPM:Transcripts per Million.



Prognostic values of dysregulated lncRNAs including RP11-89K21.1 and RP11-357H14.17 in UCEC analyzed by GEPIA. **a–i** Relationship between RP11-89K21.1 (**a**), RP11-357H14.17 (**b**), CTD-2314B22.1 (**c**), CTD-2377D24.6 (**d**), RP11-657O9.1 (**e**), LINC00668 (**f**), AP000892.6 (**g**), ACTA2-AS1 (**h**), RP11-867G23.10 (**i**) and overall survival (OS) of patients with UCEC

conclusion

In this study, 121 differentially expressed lncRNAs in UCEC were identified by circlncRNAnet, including 77 upregulated and 44 downregulated lncRNAs. We further confirmed for the first time that only high expressions of RP11-89K21.1 and RP11-357H14.17 were significantly associated with shortened OS and poor prognosis of patients with UCEC, which suggested that RP11-89K21.1 and RP11-357H14.17 played oncogene roles in the occurrence, progression of endometrial carcinoma. It was reported that the expression of lncRNAs were regulated by transcription factors [31]. We found that EZH2 was the common transcriptional regulator of RP11-89K21.1 and RP11-357H14.17 in endometrial carcinoma with AnnoLnc, Moreover, EZH2 was positively correlated with the expression of RP11-89K21.1 and RP11-357H14.17. Some studies have showed that lncRNA DLEU2 interacted with EZH2 to promote the proliferation, migration and invasion of hepatocellular carcinoma, thus accelerating the malignant progression of hepatocellular carcinoma [32]. In gastric cancer, lncRNA UCA1 enhanced the translation of cyclin D1 via recruiting EZH2 and further precipitated the proliferation and cell cycle progression of gastric cancer [33]. In lung cancer, the expression of lncRNA-SVUGP2 could be suppressed by EZH2 and further promoted the occurrence and development of lung cancer via Wnt/β-catenin pathway [34]. These studies suggest that there exists potential regulatory mechanism between EZH2 and RP11-89K21.1, RP11-357H14.17 involved in the occurrence and development of endometrial carcinoma, and the specific mechanism remains to be further explored and verified.