

eRNA-IDO: a one-stop platform for identification, interactome discovery and functional annotation of enhancer RNAs

Yuwei Zhang^{1,##}, Lihai Gong^{3,##}, Ruofan Ding³, Wenyuan Chen³, Hao Rong⁴, Yanguo Li⁵,

Fawziya Shameem², Korakkandan Arshad Ali², Lei Li^{3,*}, Qi Liao^{2,*}

¹Biomedical Big Data Center, the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, China

²School of Public Health, School of Medicine, Ningbo University, Ningbo, 315211, China

³Institute of Systems and Physical Biology, Shenzhen Bay Laboratory, Shenzhen, 518107, China

⁴School of Clinical Medicine, School of Medicine, Ningbo University, Ningbo, 315211, China

⁵Institute of Drug Discovery Technology, Ningbo University, Ningbo, 315211, China

^{##}These authors contributed equally to this work.

^{*}Co-corresponding authors.

E-mail: liaoqi@nbu.edu.cn (Qi Liao); lilei@szbl.ac.cn (Lei Li)

Abstract

Increasing evidence proves the transcription of enhancer RNA (eRNA) and its important role in gene regulation. However, we are only at the infancy stage of understanding eRNA interactions with other biomolecules and the corresponding functionality. To accelerate eRNA mechanistic study, we present the first integrative computational platform for human eRNA identification, interactome discovery, and functional annotation, termed eRNA-IDO. eRNA-IDO comprises two modules: eRNA-ID and eRNA-Anno. Functionally, eRNA-ID identifies eRNAs from *de novo* assembled transcriptomes. The bright spot of eRNA-ID is indeed the inclusion of 8 kinds of enhancer makers, whose combination enables users to personalize enhancer regions flexibly and conveniently. In addition, eRNA-Anno provides cell/tissue specific functional annotation for any novel and known eRNAs through discovering eRNA interactome from the prebuilt or user-defined eRNA-coding gene networks. The pre-built networks include GTEx-based normal co-expression networks, TCGA-based cancer co-expression networks, and omics-based eRNA-centric regulatory networks. Our eRNA-IDO carries sufficient practicability and significance for understanding the biogenesis and functions of eRNAs. The eRNA-IDO server is freely available at http://bioinfo.szbl.ac.cn/eRNA_IDO/.

Key words:

Enhancer RNA, identification, interactome, functional annotation

Introduction

The past decade has seen increasing evidence confirming the pervasive transcription of noncoding RNA from active enhancer regions, termed enhancer RNA (eRNA). Due to the dynamic nature of enhancer activity across different tissues and lineages, eRNA transcription shows high specificity to biological contexts [1]. eRNAs, once regarded as “transcription noise” or “byproduct” [2], have now been widely validated to play important roles in diversified biological functions and diseases such as cardiovascular development [3] and cancer [4]. Mechanistically, eRNA can promote enhancer-promoter loops and regulate epigenetics through interacting with several general factors, including components of cohesion or mediator [5, 6], and histone acetyltransferases CBP/p300 [4, 7]. In addition, the interaction of eRNAs with transcription elongation factors can facilitate the pause-release of RNA polymerase II pause-release to control transcription elongation.

Due to the increasing attention to eRNA functionality, several databases have been designed to characterize the transcription and potential targets of eRNAs, such as HeRA [8], TCeA [9], Animal-eRNADB [10], and eRic [11]. However, these databases only provided information on annotated eRNA loci and enhancer regions, where users cannot investigate novel eRNAs. Furthermore, despite the existence of many ncRNA functional annotation platforms, they are not well-suited to eRNAs. For example, ncFANs v2.0 [12] requires known ncRNA identifiers as input, but in fact eRNAs have no reference ID or symbol. AnnoLnc2 [13] predicts the functions of novel lncRNAs based on co-expression networks. Still, neither considers cell/tissue specificity nor provides the eRNA-specific characteristics such as histone modification, chromatin architecture, and interactive molecules. Until now, a comprehensive platform for eRNA functional annotation is still lacking.

Therefore, we present the first one-stop platform for human eRNA identification, interactome discovery, and functional annotation, termed eRNA-IDO (**Figure 1**). eRNA-IDO comprises two available modules: eRNA-ID and eRNA-Anno. eRNA-ID enables users to define enhancers and identifies enhancer-derived noncoding RNAs from the uploaded *de novo* assembled transcriptome. eRNA-Anno predicts eRNA functions by discovering eRNA-connected protein-coding genes (PCGs) in normal/cancer co-expression and eRNA-centric regulatory networks. All functions of eRNA-IDO can be realized based on pre-built data and also allow for user-defined data, thus

carrying sufficient practicability and convenience for biological researchers. This web server is freely available at http://bioinfo.szbl.ac.cn/eRNA_IDO/ and opens to all users, without a login requirement.

Materials and Methods

Workflow and data architecture of eRNA-ID

The left panel of **Figure 1** shows the schematic workflow of eRNA-ID. eRNA-ID takes *de novo* assembled transcripts of RNA-seq or GRO-seq data provided by users as input. The transcripts overlapped with annotated PCGs, simple repeats, and blacklisted regions are removed according to the GENCODE v33 reference [14]. Next, the coding potential of the remaining transcripts is evaluated by CPC2 [15] (default parameter), and noncoding RNAs transcribed from enhancer regions are predicted as eRNAs. Enhancer regions can be either uploaded by users in BED format or defined using our marker buffet. The marker buffet is composed of 8 kinds of enhancer markers, including H3K27ac (**Supplementary Table S1**), H3K4me1 (**Supplementary Table S2**), chromatin accessibility (**Supplementary Table S3**), RNA polymerase II binding (**Supplementary Table S4**), super-enhancers from SEdb v2.0 [16], EnhancerAtlas v2.0 [17] enhancers, FANTOM5 [18] enhancers and SCREEN/ENCODE [19] enhancers, which are optionally overlapped or merged (using bedtools multiinter/merge) to obtain high-confidence or comprehensive enhancer profiles. The +/-3 kb regions around the center of the selected markers are defined as potential enhancer regions. These markers are cell/tissue-specific except those from FANTOM5 and SCREEN database. The data type, source, and number of biosamples of these enhancer markers are listed in **Table 1**. Finally, eRNA-ID outputs the chromatin locations, adjacent genes (+/- 1Mb), and enhancers of predicted eRNAs.

Workflow and data architecture of eRNA-Anno

The right panel of **Figure 1** shows the schematic workflow of eRNA-Anno. eRNA-Anno takes either chromatin coordinates of novel eRNAs or the identifiers of known eRNAs annotated in HeRA [8] and eRic [11] database as input. Novel eRNAs should be input in BED or GTF format. For known eRNAs, the ENSR identifiers, chromatin coordinates, and adjacent genes (within

$\pm 1\text{Mb}$) are acceptable. Below is the detailed description for each procedure.

1. *eRNA quantification*

The expression levels of known eRNAs are obtained from HeRA and eRic. Suppose chromatin coordinates of novel eRNAs serve as input, in that case, RNA-seq data from TCGA (<https://portal.gdc.cancer.gov/>) and GTEx portal [20] are used to quantify eRNA expression. To save the processing time, the expression levels are estimated based on the read coverage from BigWig files. The formula is:

$$FPKM = \frac{\sum(Cov) \times 10^9}{R \times L \times T}$$

Where $\sum(Cov)$ is the total read coverage of a given eRNA region, R is read length, L is eRNA length, and T is the total mapped reads of the library.

2. *Profiling genetic/epigenetic landscape*

eRNA-Anno portrays a genetic/epigenetic landscape for eRNAs, including chromatin accessibility, clinically relevant mutation, and histone modification (H3K27ac and H3K4me1). Histone modification and chromatin accessibility are characterized based on ChIP-seq and ATAC-seq/DNase-seq from Cistrome database [21] (**Supplemental Table 1-3**). Clinically relevant mutations within the query eRNA regions are collected from ClinVar [22] and COSMIC [23] database.

3. *eRNA-PCG network construction*

eRNA-Anno constructs a co-expression network between eRNAs and PCGs and an eRNA-centric regulatory network. Both user-uploaded expression matrix and publicly available data are supported for the co-expression network. Publicly available data refer to RNA-seq data of 52 normal tissues from GTEx portal [20] and 31 cancer types from the TCGA portal (**Supplementary Table S5**). The toolkit GCEN [24] calculates Spearman correlation coefficients and adjusted p-values.

For the eRNA-centric regulatory network, the relationships of eRNAs with TF, RBP, and E-P loop are investigated. eRNA-TF interactions are obtained based on 11356 ChIP-seq datasets from Cistrome database [21], which involve 1354 TFs and 642 cells/tissues (**Supplementary Table S4**). eRNA-RBP interactions are obtained based on 518 CLIP-seq datasets from POSTAR3 database [25], which involve 221 RBPs and 34 cells/tissues (**Supplementary Table S6**). TFs and RBPs

with peaks located within eRNA regions are defined as potential regulators of eRNAs. E-P loops identified by 200 HiChIP experiments across 108 cell types (**Supplementary Table S7**) are collected from HiChIPdb [26]. The loops harboring anchors overlapped with query eRNAs are defined as eRNA-mediated loop.

4. Subnetwork extraction

eRNA-Anno extracts hubs/modules from the overall network to obtain the tightly connected PCGs of query eRNAs. Module extraction uses SPICi [27] in the unweighted mode (default parameter).

5. Functional enrichment analyses

Functional enrichment analyses, including gene ontology (GO), KEGG pathway, and MSigDB hallmark enrichment [28], are performed based on hypergeometric test using our in-house scripts (<https://github.com/zhangyw0713/FunctionEnrichment>).

Results

eRNA-ID for eRNA identification

eRNA-ID is designed for eRNA identification based on *de novo* assembled transcriptome. As shown in the input interface (http://bioinfo.szbl.ac.cn/eRNA_ID/eRNA-ID), users need to upload a transcriptome profile in GTF format, which can be generated from RNA-seq and GRO-seq data, and define enhancer regions using our marker buffet or by uploading their BED file. eRNA-ID adopts the similar analytical workflow used in ncFANS-eLnc [12] to predict eRNAs (see **Materials and Methods**). The major advantage of eRNA-ID compared to ncFANS is the inclusion of a pre-built buffet of 8 kinds of enhancer markers (H3K27ac, H3K4me1, chromatin accessibility, RNA polymerase II binding, SEdb v2.0 super-enhancers, and three types of enhancer annotations from EnhancerAtlas v2.0 [17], FANTOM5 [18], and SCREEN [19] databases), which enables users to personalize enhancer regions of their interests. For example, users may require high-confidence enhancer regions simultaneously labeled by multiple markers or want to obtain as many enhancers as possible by merging all markers. The processing procedure of eRNA-ID is fast; a GRO-seq derived transcriptome with 3483 transcripts (SRA008244) and a total RNA-seq derived *de novo* transcriptome with 222,848 transcripts (GSM2824220) cost 45 and 88 seconds respectively (default parameters).

In the output interface of eRNA-ID (**Figure 2**), a table showing chromatin coordinates,

enhancers, and putative targets (adjacent genes within +/- 1Mb of eRNAs) of predicted eRNAs is provided. Users can also view the information in a genome browser based on JBrowse [29]. Moreover, users can conduct functional annotation for these novel eRNAs by clicking on the “Deliver eRNA to eRNA-Anno” button.

eRNA-Anno for interactome discovery and functional annotation

eRNA-Anno is designed for the network-based interactome discovery and functional annotation of eRNAs. In this module, users need to input either chromatin coordinates of novel eRNAs (**Figure 3A**) or the identifiers/locations of known eRNAs annotated in the HeRA [8] and eRic [11] database (**Figure 3B**), followed by network selection and parameter setting. eRNA-Anno first quantifies the eRNA expression levels based on RNA-seq data from TCGA and GTEx portal. As hundreds of RNA-seq samples take long processing time, we used the read coverages from BigWig files to speed up the quantification (see **Materials and Methods**). To examine the reliability of this method, we correlated the expression levels of known eRNAs based on this method with those based on canonical method and obtained from HeRA and eRic database. As expected, our method is highly correlated with canonical method using featureCounts [30] (**Figure S1A-B**) and is approximately 400 times faster (**Figure S1C**).

Next, eRNA-IDO annotates the functions of eRNAs through discovering their interactomes. Interactome discovery is based on the eRNA-centric networks. Networks include normal co-expression networks based on GTEx expression profiles [20], cancer co-expression networks based on TCGA expression profiles (<https://portal.gdc.cancer.gov/>), and eRNA-centric regulatory networks. Co-expression relationships have been widely used to annotate the functions of eRNAs [31-33]. Additionally, eRNAs were reported to exert regulatory functions through interacting with other biomolecules, including transcription factors (TFs) [34-36], RNA binding proteins (RBPs) [4, 37, 38], and target gene activated by E-P loops [39, 40]. These interactions make the regulatory network a powerful tool for eRNA functional annotation, resembling to those we used for other ncRNAs [12, 41-44]. The procedure of network construction is shown in **Materials and Methods**. Parameters include tissue/cancer type of expression profile, co-expression coefficient, significance threshold, biosamples of interaction relationships, and epigenetic landscape (**Figure 3C-D**).

Once receiving launch instruction, eRNA-Anno will initiate the analytical procedure (see

Material and Methods) to discover the potential targets of query eRNAs from the selected networks and annotate their functions based on the hub- and module-based strategies. The whole procedure will take tens of minutes, depending on the number of the input eRNAs (**Figure. S2**). Therefore, we highly recommend users to set an email notification or record the task ID for result retrieval, when a task with a large set of eRNAs is submitted.

In the output interface, eRNA-Anno provides basic information about eRNAs (i.e., location and expression, epigenetic landscape, and disease relevance) and putative targets and functions based on different networks. In the section of “location and expression” chromatin coordinate, the expression level in normal and cancer samples, adjacent genes (<=1Mb), and overlapped super-enhancers are listed in the table (**Figure 4A**). To evaluate the activity of enhancers where eRNA is transcribed, eRNA-Anno profiles active enhancer markers (H3K27ac and H3K4me1) and chromatin accessibility of eRNA regions (**Figure 4B**). Given that mutations in eRNA regions are always related to eRNA expression and subsequent disease development [45], the clinically relevant mutations within query eRNA regions are shown (**Figure 4C**). The interactome and predicted functions of eRNAs based on the selected networks are displayed in the second part (**Figure 5**). For example, in a cancer co-expression network (**Figure 5A**), the eRNA-PCG network is visualized in a force-directed layout, and the functions of connected PCGs are provided (**Figure 5B**). Since genes with similar functions tend to be concentrically distributed, eRNA-Anno extracts hubs and modules composed of tightly connected genes from the overall network (**Figure 5D**). The function of query eRNAs can be inferred by the functions of the PCGs within the same module or hub (**Figure 5C**).

Moreover, for the eRNA-centric regulatory network (**Figure 5E**), the relationships of eRNAs with TFs, RBPs, and E-P loops are visualized in multiple modes, including network, table, and genome browser. Similarly, the functions of eRNAs can be inferred by the related biomolecules in the overall network, modules, or hubs. After obtaining the results based on individual networks, users can combine them to get a summary (**Figure 6**).

A case study to showcase the usage of eRNA-Anno

As the input interface has many user-dependent options and the output interface displays interactive information, we show a case to well understand the usage and interpretation of results

obtained from eRNA-Anno. CCAT1 and LINC02257, characterized as colon cancer-associated eRNAs [46, 47], were used in this study. We input them in GTF format, selected “TCGA-COAD” and “GTEx-Colon Transverse” in eRNA quantification, chose co-expression and regulatory networks, set parameters, and finally launched eRNA-Anno, as shown in **Figure 3**.

In the output interface, eRNA-Anno showed that both CCAT1 and LINC02257 exhibit higher expression levels in colorectal cancer (**Figure 4A**) and are enriched with active enhancer markers (**Figure 4B**), which is in line with the published studies [46, 47]. In addition, CCAT1 and LINC02257 regions harbor carcinoma-associated mutations (**Figure 4C**), indicating their clinical significance. To evaluate the interactome and functions of CCAT1 and LINC02257, we next looked into the co-expression network in colon adenocarcinoma. The topology of the co-expression network showed limited connections between CCAT1 and LINC02257 (**Figure 5A**), indicating their large independence in regulating target gene expression. Besides, functional enrichment analysis on the co-expressed protein-coding genes demonstrated that CCAT1 and LINC02257 are potentially enriched for translation and cell cycle pathways (**Figure 5B**). The module involved in CCAT1 precisely pinpointed the role of CCAT1 in regulating the cell cycle (**Figure 5C-D**), which conforms to previous finding [48, 49]. Moreover, the eRNA-centric regulatory network detected the interactive TFs, RBPs and the genes targeted by E-P loops, and simultaneously revealed the potential functions of CCAT1 and LINC02257 in cell cycle and cancer pathways. To intuitively visualize eRNA locations and the mutational, epigenetic and interactive landscapes, a genome browser based on JBrowse [29] was provided (**Figure 5E**). Finally, we overlapped the nodes and edges between the eRNA-centric regulatory network and cancer co-expression network. We discovered high-confidence interactions of CCAT1 in a cell cycle-related module (**Figure 6**), of which some targets such as CDK4 [50] and SOX4 [51] had been reported. This case study exemplifies the potential of eRNA-Anno, showing how it can provide comprehensive and reliable prediction on eRNA interactome and functions.

Discussion

As a web server dedicated for eRNA, eRNA-IDO endows eRNA identification, interactome discovery and functional annotation in a convenient manner. The major advantage of eRNA-IDO

include but are not limited to the below:

- 1) eRNA-ID provides a combination of multiple enhancer markers to realize convenient and personalized definition of enhancer regions. Compared to ncFANs-eLnc [12] with only H3K27ac marker, eRNA-ID includes 8 kinds of enhancer markers.
- 2) eRNA-Anno serves for any novel and known eRNAs. Considering the poor characterization of eRNAs, the applicability to novel eRNAs endows eRNA-Anno with higher flexibility and biological practicability compared to other tools requiring known identifiers such as ncFANs [12] and the databases [8-11].
- 3) Biological context-specific expression and interaction profiles are pre-built in eRNA-Anno. Comparing to the tools without biological specificity such as AnnoLnc2 [13], eRNA-Anno is expected to provide more precise clues for the *in vivo* investigations. Also, the pre-built profiles enable the service in a more convenient and expedite manner.
- 4) eRNA-IDO is the first one-stop platform for eRNA identification, interactome discovery, and functional annotation.

We also acknowledge that there remain some drawbacks and will put continuous effort to overcome them. First, our eRNA-IDO is currently designed for human data. More species will be supported in future. Second, further characteristics of eRNAs such as m⁶A modification [52] and RNA structure [53, 54] are essential for eRNA functionality but have not been investigated by eRNA-Anno. Third, current eRNA-IDO only considers normal tissue and cancer. More disease- and cell-specific expression and interaction profiles will be incorporated. Hopefully, our eRNA-IDO will benefit from user feedback and become more powerful upon our continuous updates.

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Conflict of interest

The authors declare that they have no competing interests.

Figure

Figure 1. The workflow of eRNA-IDO. eRNA-IDO comprises two functional modules: eRNA-ID for eRNA identification and eRNA-Anno for interactome discovery and functional annotation.

Figure 2. The output interface of eRNA-ID. The predicted eRNA locations, enhancer regions, markers for active enhancers, putative targets (adjacent genes), and overlapped lncRNAs are shown in a table and can be visualized in the genome browser. More details are shown in the demo: http://bioinfo.szbl.ac.cn/eRNA_IDO/retrieve/?taskid=5a9LFXS8oGCm.

Figure 3. The input interface of eRNA-Anno, (A) including a potential eRNA list, optional target candidates, parameters for eRNA quantification, network selection, and genetic/epigenetic landscape. (B) Input interface for known eRNAs annotated in HeRA [8] and eRic [11]. (C) Parameters of co-expression network and (D) eRNA-centric regulatory network.

Figure 4. The output interface of eRNA-Anno shows the basic information of query eRNA CCAT1 and LINC02257, including (A) location and expression level, (B) epigenetic landscape, and (C) mutation-based disease relevance. (D) The genome browser can be activated by clicking on the button “Visualization in genome browser”. More details are shown in the demo: http://bioinfo.szbl.ac.cn/eRNA_IDO/retrieve/?taskid=97XPLicEAj4euYG/.

Figure 5. The output interface of eRNA-Anno shows the interactomes and functions of CCAT1 and LINC02257 based on (A) co-expression networks and (B) regulatory networks.

Figure 6. Summary of the interactome and functions of query eRNAs based on the combination of co-expression network and regulatory network. Upon (A) parameter setting, (B) a high-confidence network composed of the overlapped nodes and edges is generated for CCAT1 and LINC02257. (C) The module involved in CCAT1 indicates its interactive genes and functions in cell cycle regulation.

Table

Table 1. Data type, source, and the number of biosamples of enhancer markers

Supplementary Figures

Supplementary Figure 1. Comparison of the strategies for eRNA quantification. (A-B)

Distribution of Pearson correlation coefficients of eRNA levels quantified by our methods with those collected from (A) HeRA and (B) eRic database. (C) Comparison of the running time between our method and canonical featureCounts [30]. The test sample is GTEX-ZYFC-2626-SM-5NQ6S from GTEx database. The task was done on a Dell Precision T7920 workstation with single core.

Supplementary Figure 2. The running time of eRNA-Anno across the different eRNA numbers.

X-axis and y-axis represent the input eRNA numbers and the running time, respectively.

Supplementary Tables

Supplementary Table 1. ChIP-seq dataset of H3K27ac modification

Supplementary Table 2. ChIP-seq dataset of H3K4me1 modification

Supplementary Table 3. ATAC-seq/DNase-seq datasets of chromatin accessibility

Supplementary Table 4. ChIP-seq datasets of 1354 TFs

Supplementary Table 5. Normal tissue- and cancer-specific RNA-seq datasets

Supplementary Table 6. CLIP-seq datasets of RBPs

Supplementary Table 7. HiChIP datasets from HiChIPdb

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ERNA-ID
eRNA-ID

Home eRNA-Anno Statistics Help Contact

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Enhancer number: 137034

Novel ncRNA number: 512

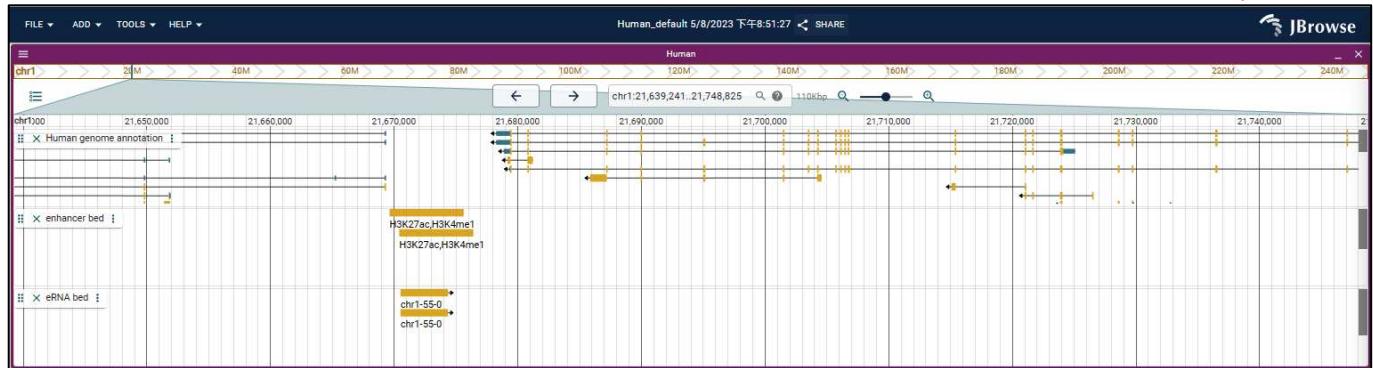
eRNA (novel ncRNA from enhancer) number: 391

Download the eRNA list Download CPC2 result

eRNA_chr	eRNA_start	eRNA_end	eRNA_ID	Strand	Enhancer_chr	Enhancer_start	Enhancer_end	Enhancer_marker	Putative targets	Overlapped known lncRNA
chr1	11052358	11054337	chr1-26-0	+	chr1	11050094	11056095	H3K4me1	View putative targets View	
chr1	16678078	16678477	chr1-39-0	+	chr1	16677590	16683591	H3K4me1	View putative targets View	
chr1	21670540	21674386	chr1-55-0	+	chr1	21669662	21675663	H3K27ac,H3K4me1	View putative targets View	
chr1	21670540	21674386	chr1-55-0	+	chr1	21670438	21676439	H3K27ac,H3K4me1	View putative targets View	
chr1	32064797	32067113	chr1-433-1	-	chr1	32063548	32069549	H3K4me1	View putative targets View	
chr1	32064797	32067113	chr1-433-1	-	chr1	32059846	32065847	H3K27ac,H3K4me1	View putative targets View	
chr1	32064797	32067113	chr1-433-1	-	chr1	32061555	32067556	H3K27ac	View putative targets View	
chr1	36386110	36386969	chr1-411-1	-	chr1	36384158	36390159	H3K27ac,H3K4me1	View putative targets View	
chr1	36453201	36455428	chr1-137-0	+	chr1	36448025	36454026	H3K27ac,H3K4me1	View putative targets View	
chr1	42172184	42175574	chr1-149-0	+	chr1	42171678	42177679	H3K4me1	View putative targets View	

913 items 1 2 3 4 5 ... 92 > 10 Go to

[Deliver eRNA to eRNA-Anno](#) [Visualization in genome browser](#)



Zhang Y and Gong L et. al. Figure 3**A**

Novel eRNA Known eRNA **Move to input page for known eRNA**

User input

1. Input query eRNA list in the below box [load example](#)

GTF BED

Click or drag file to this area to upload

2. Input candidate **target genes** to constrain the network (Optional) [load example](#)

Click or drag file to this area to upload

Expression quantification

Please choose or upload the expression profiles for the eRNA expression quantification and co-expression network construction

Based on the preconstructed expression profile

Cancer TCGA/COAD

Normal Colon_Transverse

or users upload the expression profiles (both below are required) [load example](#)

1.eRNA expression profile

2.Expression of potential targets

Click or drag file to this area to upload

Click or drag file to this area to upload

Network Selection

> Normal and cancer co-expression network YES

> Regulatory relationships YES

Genetic/Epigenetic landscape

> Epigenetic feature YES

> Mutation and Disease relevance YES

Run

B

Novel eRNA Known eRNA

User input

*Input the query eRNA in the box below [load example](#) or upload the list via the button [upload](#)

ENSR_ID Chromatin_coordinate Adjacent_gene

Input eRNAs in following format:
ENSR00000032472
ENSR000000261094
ENSR000000261096
ENSR00000032520

Or for chromatin coordinates:
chr5:150917700-150923700
chr9:63104200-63110200

C

Network Selection

> Normal and cancer co-expression network YES

NOTE: The co-expression network construction is based on the expression profile you **selected / uploaded** in above "Expression quantification" section

Advanced options (optional, set network parameters)

Correlation coefficient between eRNA and protein-coding gene: 0.4

Correlation coefficient between two protein-coding genes: 0.7

Significant threshold FDR: 0.05

D

Regulatory relationships

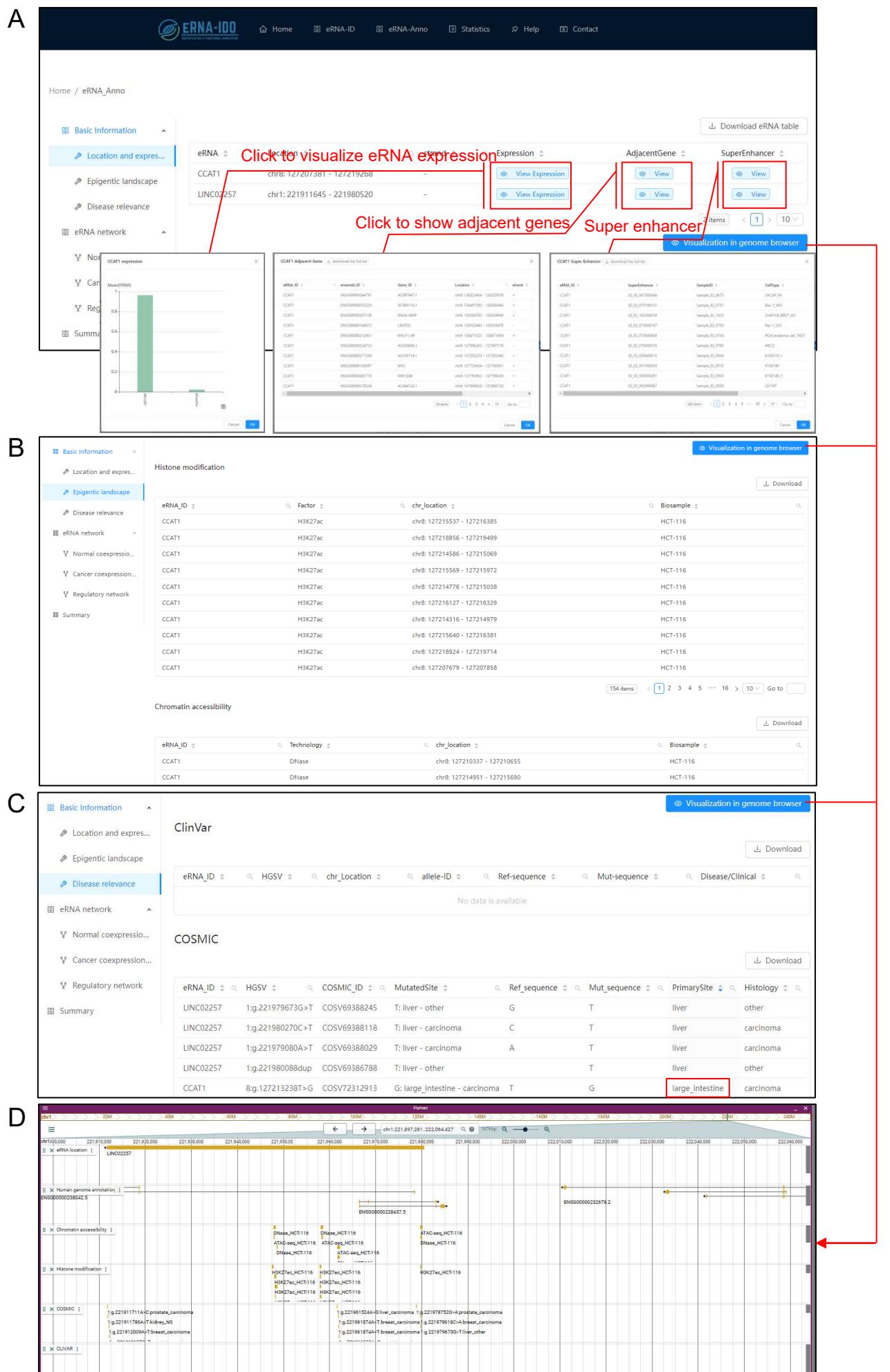
Transcription factor Overall / Overall

RNA binding protein Overall / Overall

Enhancer-promoter loop Overall / Overall

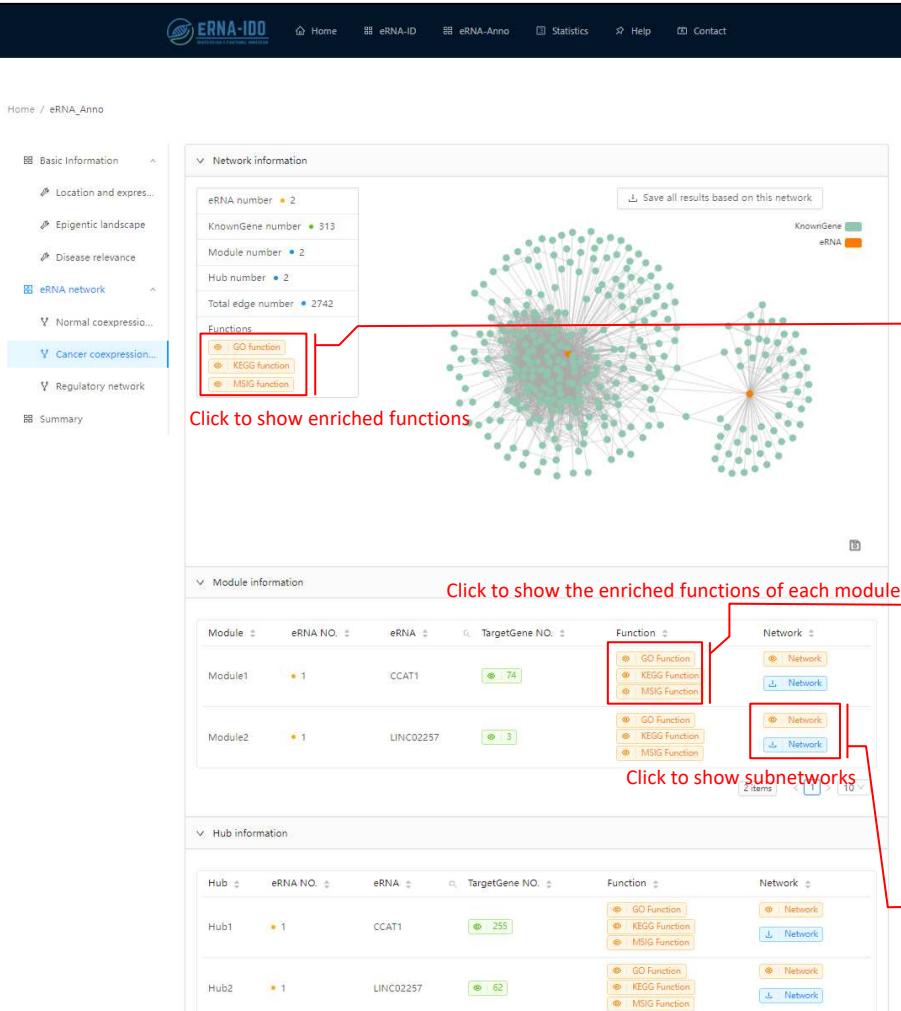
Choose biosample

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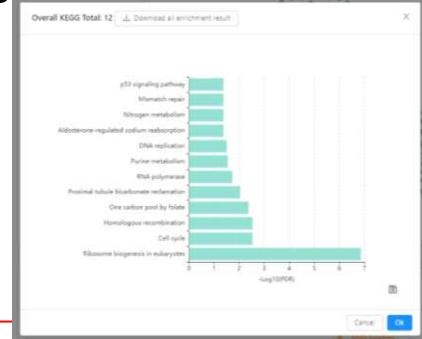


Zhang Y and Gong L et. al. Figure 5

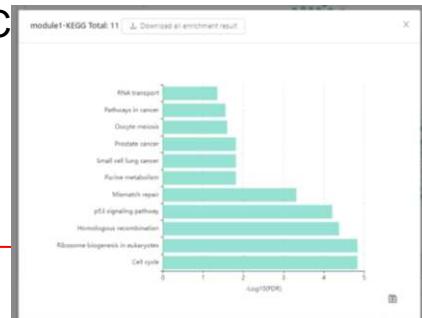
A



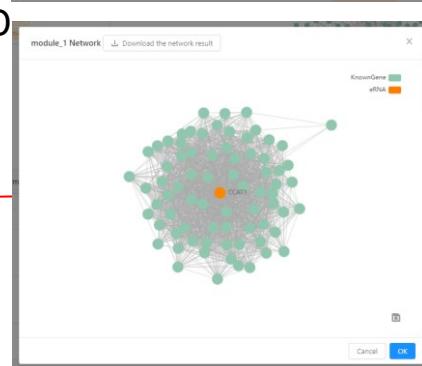
B



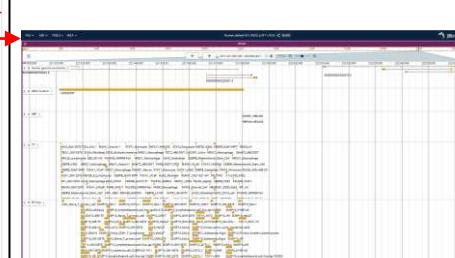
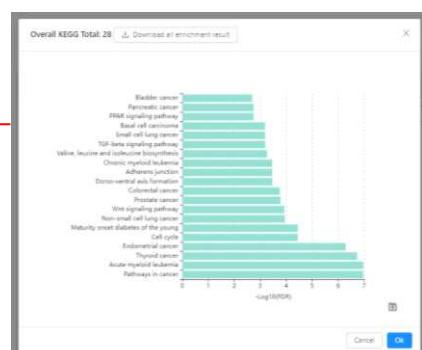
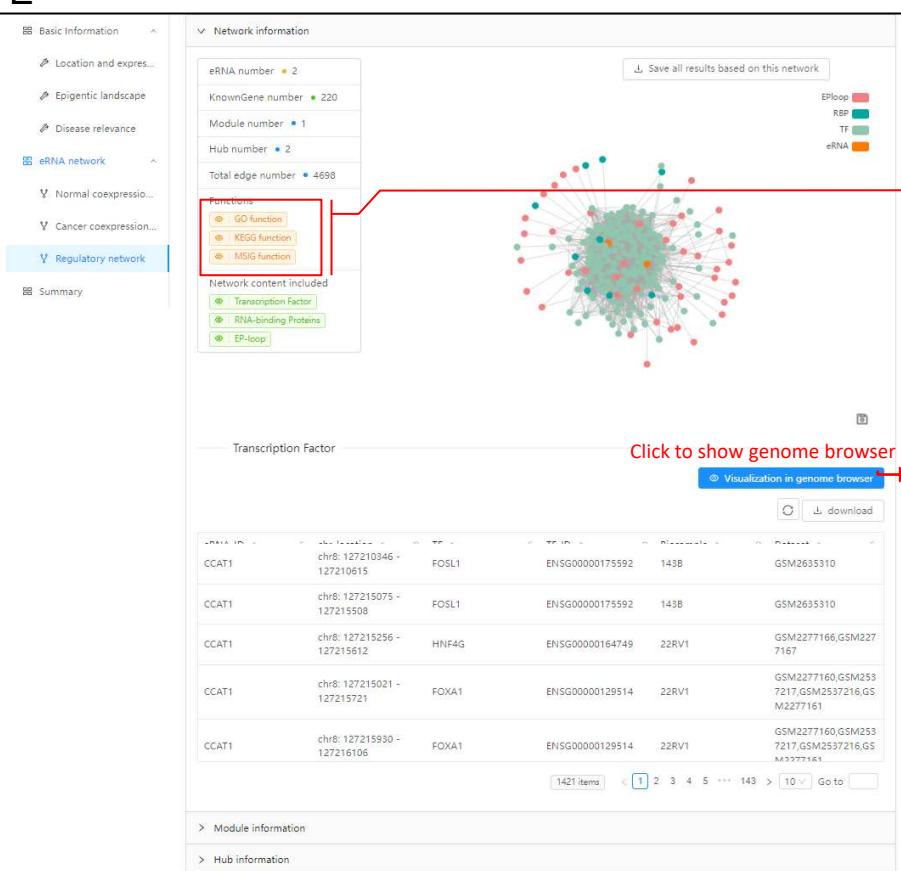
C



D



E



A

ERNA-IDO

Home / eRNA_Anno

Basic Information

- Location and expression
- Epidemic landscape
- Disease relevance

eRNA network

- Normal coexpression
- Cancer coexpression
- Regulatory network

Summary

Combine the networks to summarize the potential interactome and functions of eRNAs

Select Network

Regulatory network

Co-expression

Normal Cancer

Target-Target Interaction

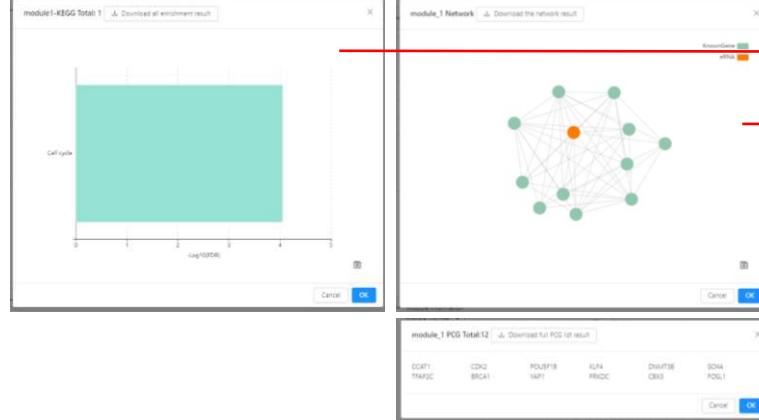
Target-target co-expression

PPI from STRING

Coexp-PPI overlap

Coexp-PPI merge

Merge Overlap

C**B**

Combine is completed.

Network information

eRNA number: 2
KnownGene number: 15
Module number: 1
Hub number: 2
Total edge number: 63

Functions

GO function

KEGG function

MSGG function

Save all results based on this network

Module information

Module: 1 eRNA NO.: 1 eRNA: CCAT1 TargetGene NO.: 14 Function: GO Function Network: Network

Module: 1 eRNA NO.: 1 eRNA: CCAT1 TargetGene NO.: 14 Function: KEGG Function Network: Network

Module: 1 eRNA NO.: 1 eRNA: CCAT1 TargetGene NO.: 14 Function: MSGG Function Network: Network

Click to show enriched functions

Click to show subnetworks

Hub information

Hub: 1 eRNA NO.: 1 eRNA: CCAT1 TargetGene NO.: 14 Function: GO Function Network: Network

Hub: 1 eRNA NO.: 1 eRNA: CCAT1 TargetGene NO.: 14 Function: KEGG Function Network: Network

Hub: 1 eRNA NO.: 1 eRNA: CCAT1 TargetGene NO.: 14 Function: MSGG Function Network: Network