

circRNA研究策略 及相关技术

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nature
materials

Circulating tumour DNA methylation markers for diagnosis and prognosis of hepatocellular carcinoma

徐瑞华教授（中山大学肿瘤防治中心），张康教授（加州大学）及其团队

该研究结果证实，可以通过检测少量血液中循环肿瘤DNA（ctDNA）特定位点甲基化水平，在早期诊断和预后预测肝细胞癌。

Science
Translational
Medicine

18 OCTOBER 2017



AAAS

Aristolochic acids and their derivatives are widely implicated in liver cancers in Taiwan and throughout Asia

Alvin W. T. Ng^{1,2,3,*}, Song Ling Poon^{4,*}, Mi Mi Huang^{1,2}, Jing Quan Lim^{4,5}, Arnoud Boot^{1,...}

* See all authors and affiliations

论文通过病理标本测序的方法，证明在亚洲（特别是台湾、中国大陆），肝癌的发生与马兜铃酸导致的突变密切相关。

- TUMOR INHIBITORS. I. ARISTOLOCHIC ACID, THE ACTIVE PRINCIPLE OF ARISTOLOCHIA INDICA.
(PMID:14056399)

[Abstract](#)[Citations](#)[BioEntities](#)[Related Articles](#)[External Links](#)

[KUPCHAN SM](#), [DOSKOTCH RW](#)

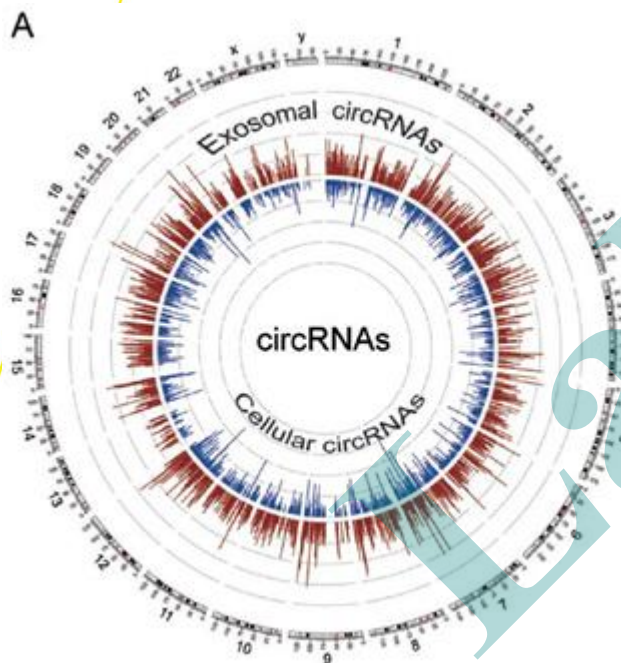
[Journal of Medicinal and Pharmaceutical Chemistry](#) [01 May 1962, 91:657-659]

Type: Journal Article

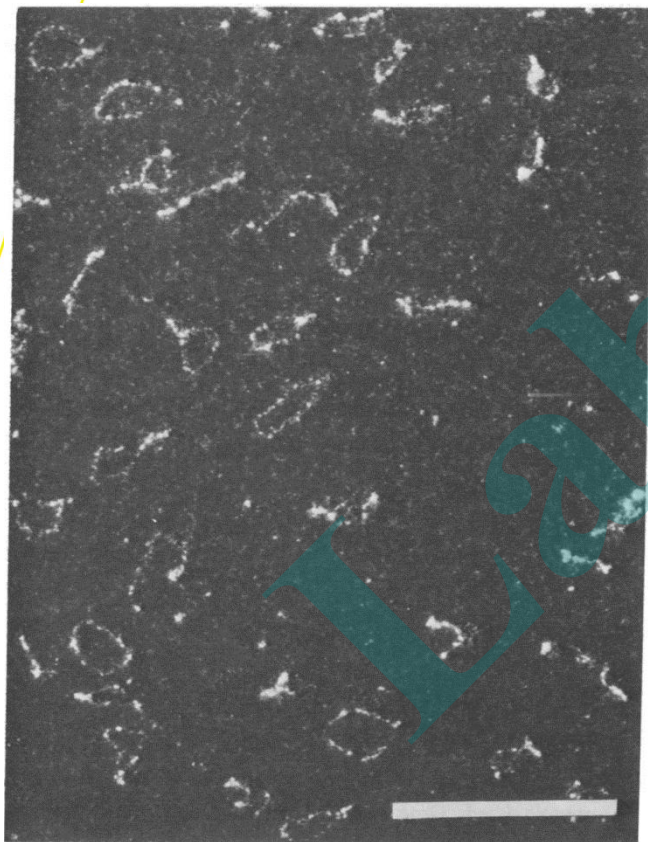
Abstract

No abstract provided.

- 1. circRNA概况
- 2. circRNA研究思路
- 3. circRNA主流数据库
- 4. 常用相关技术



- circRNAs (Circular RNAs, 环形RNA分子) 是一类不具有5'末端帽子和3'末端poly(A)尾巴、并以共价键形成环形结构的, 而且是客观存在于生物体内的非编码RNA分子。



Viroids are single-stranded covalently closed circular RNA molecules existing as highly base-paired rodlike structures. Proc. Natl. Acad. Sci. (1976)

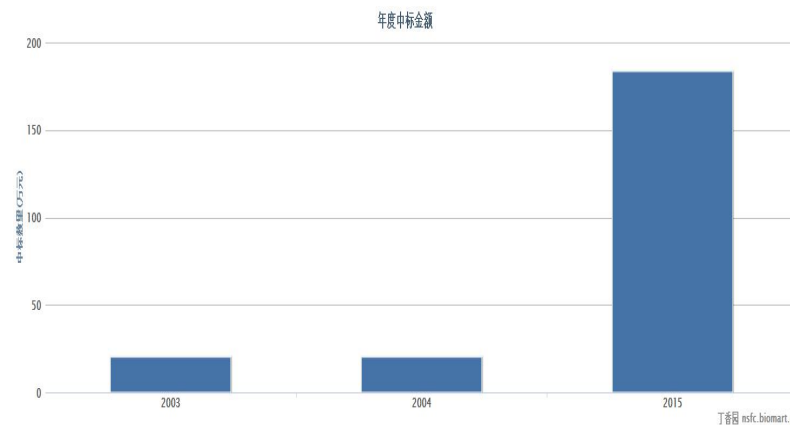
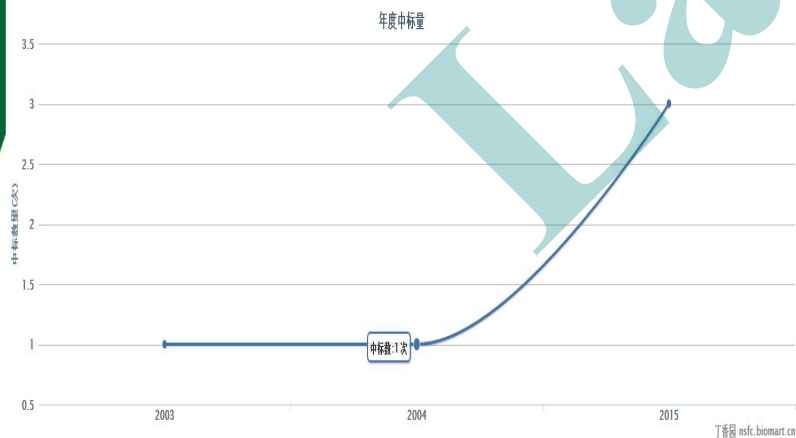
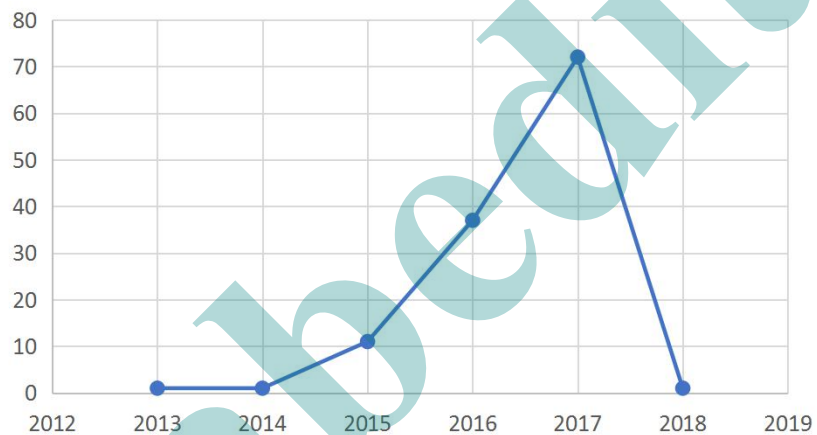
Circular RNAs are a large class of animal RNAs with regulatory potency. **Nature . (2013)**

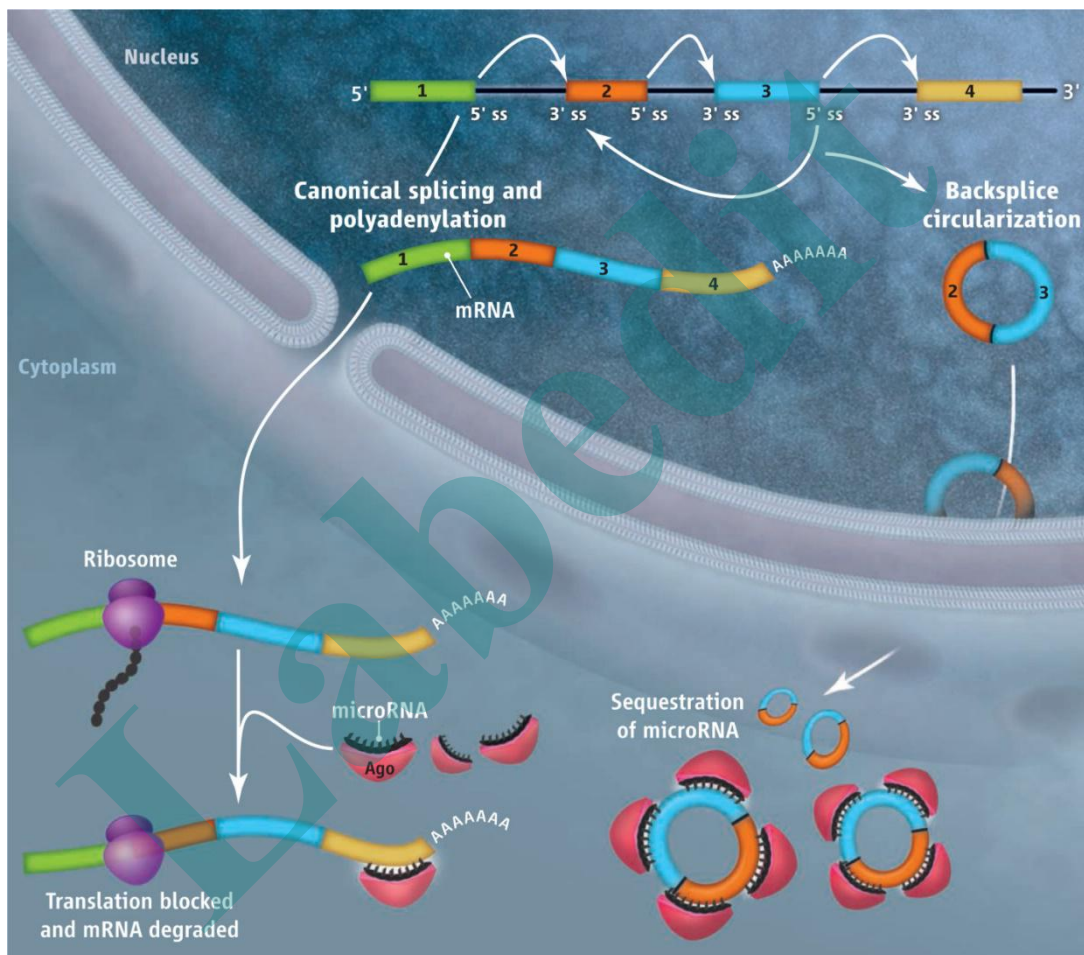
Natural RNA circles function as efficient microRNA sponges. **Nature. (2013)**

Complementary Sequence-Mediated Exon Circularization . **Cell (2014)**

Exon-intron circular RNAs regulate transcription in the nucleus. **Nature structural & molecular biology .(2015)**

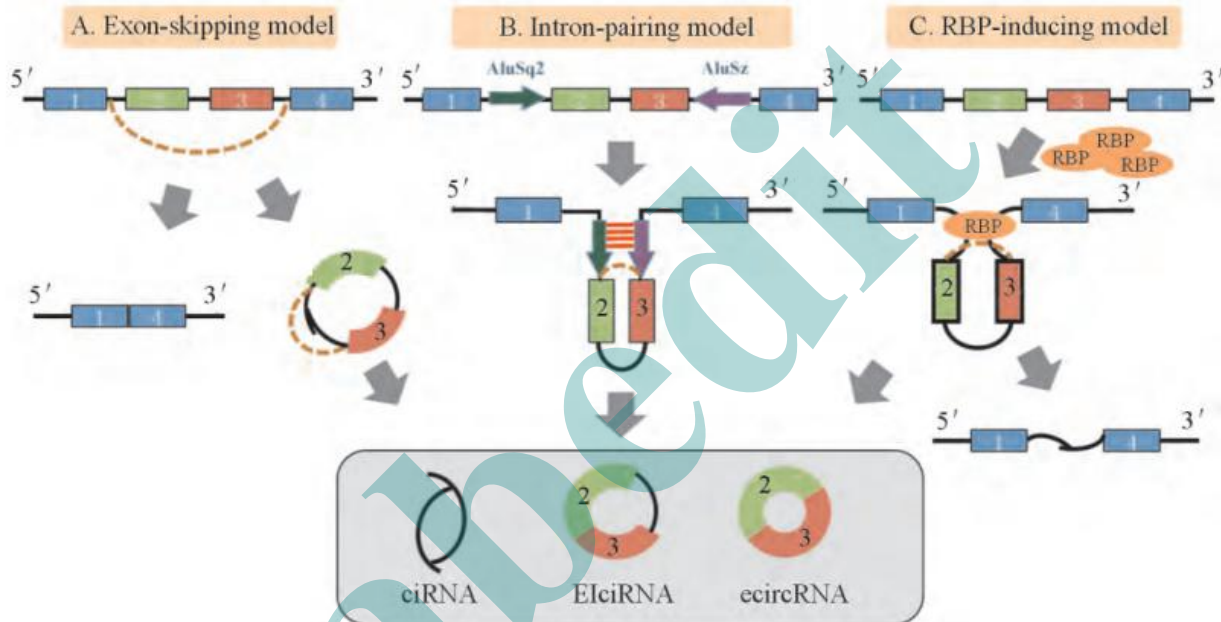
Circular RNAs in the mammalian brain are highly abundant, conserved, and dynamically expressed. **Molecular cell, 2015.**





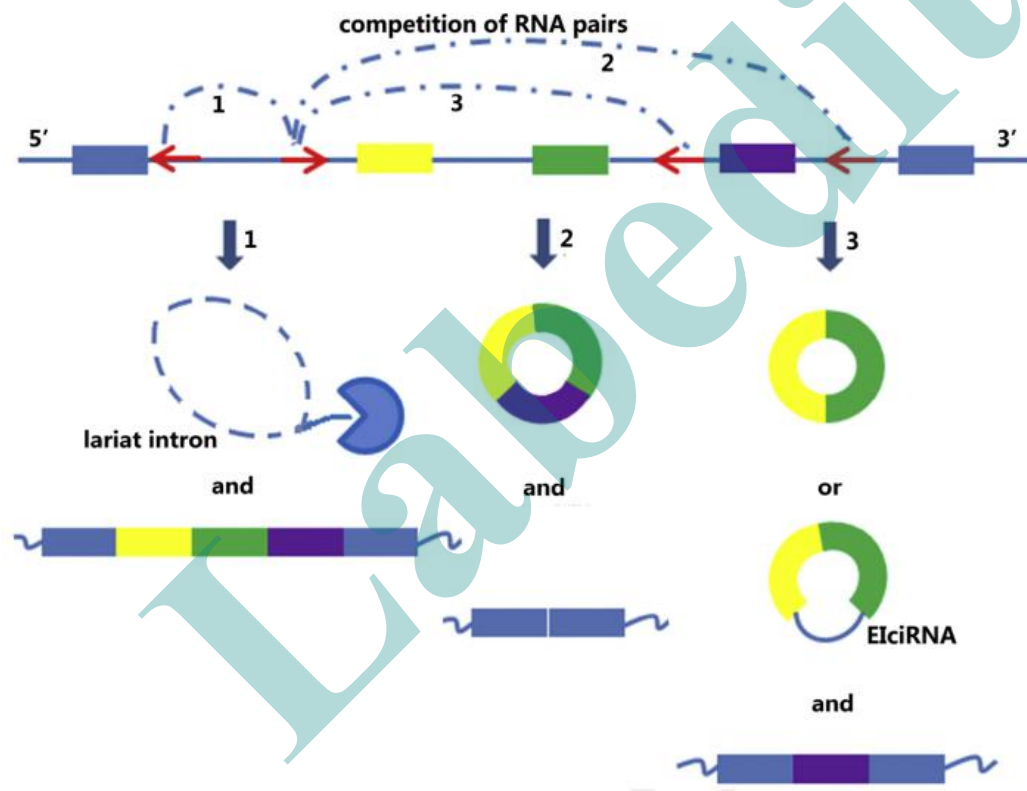
circRNA可定位于胞质或胞核参与调控作用。

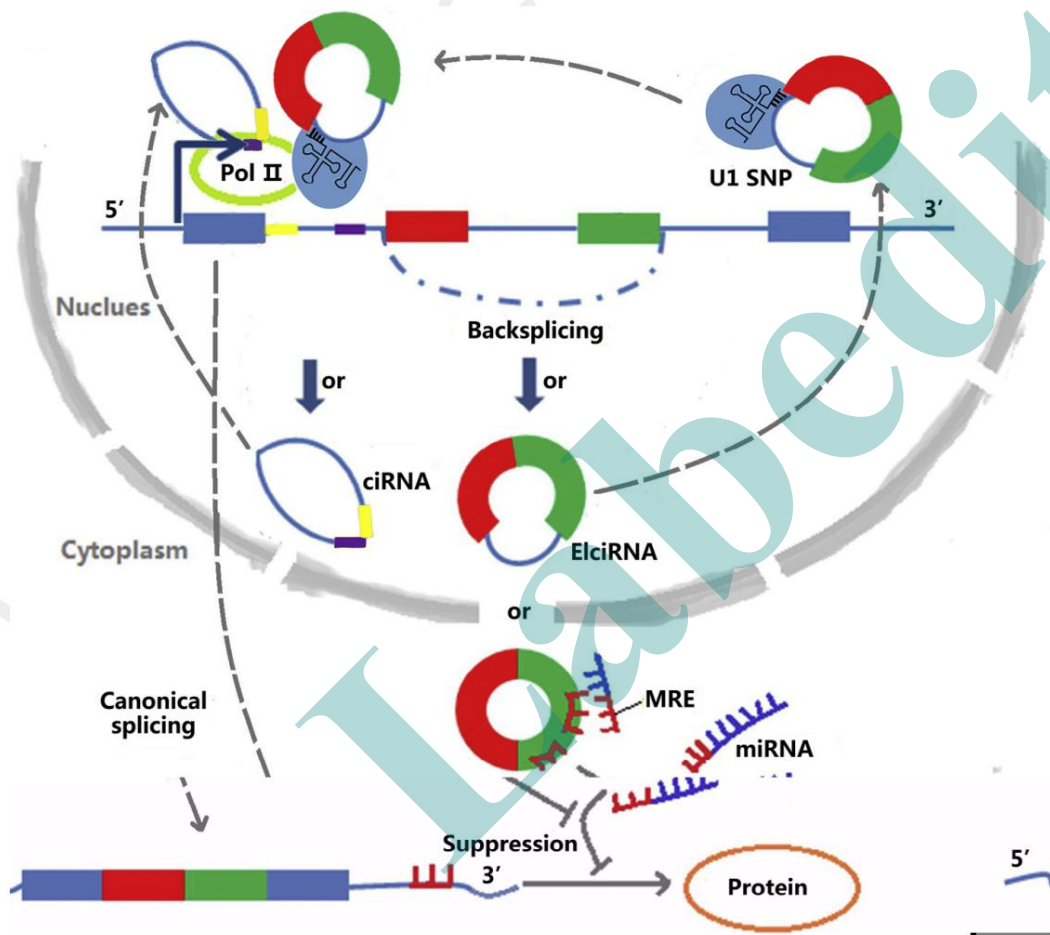
环状RNA 环化模式



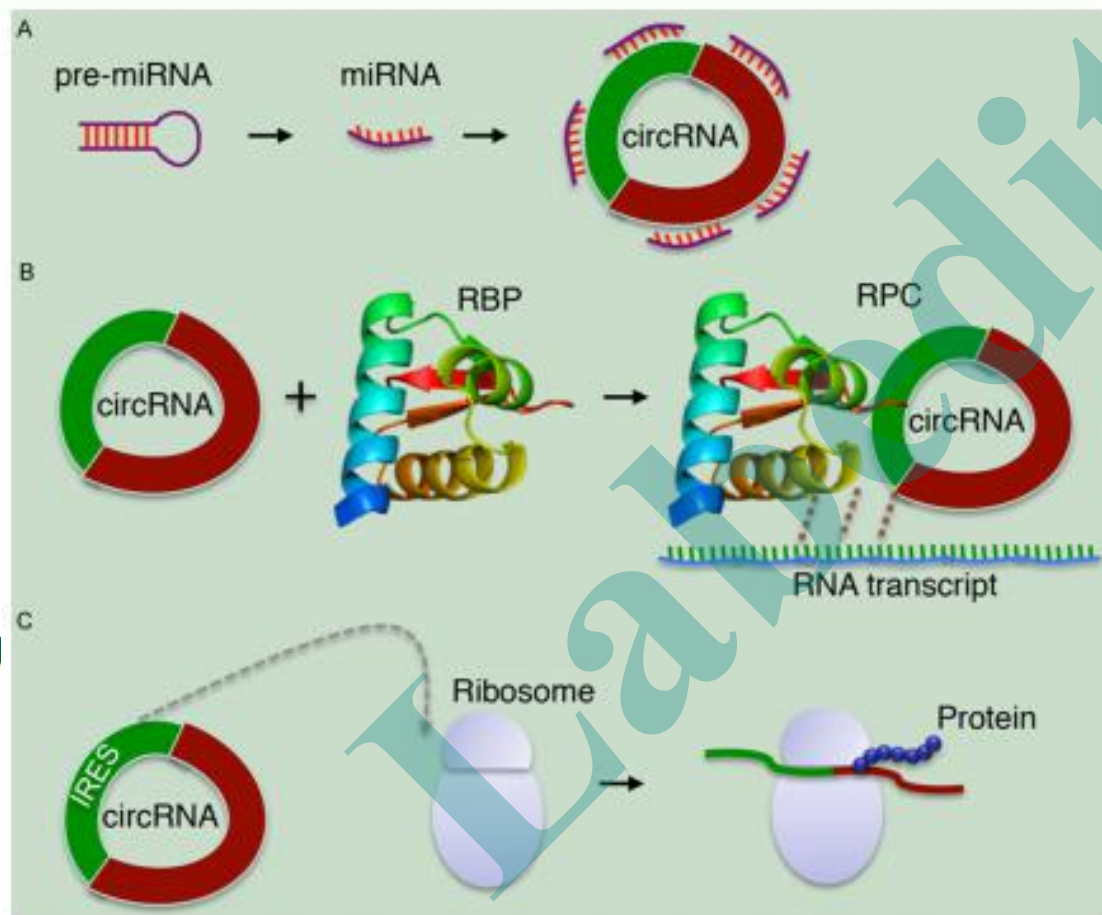
内含子circRNA
 外显子circRNA
 内含子-外显子circRNA

三类circRNA的形成过程模式





1. 内含子circRNA通过与RNA聚合酶II结合后，参与母基因的转录调控；
2. 内含子和外显子混合形成的circRNA（ElciRNA）通过与核小RNA结合后，再和其他转录调控元件形成复合体，共同参与转录调控；
3. 外显子circRNA能通过核孔转运到胞质后，吸附miRNA行使海绵功能。

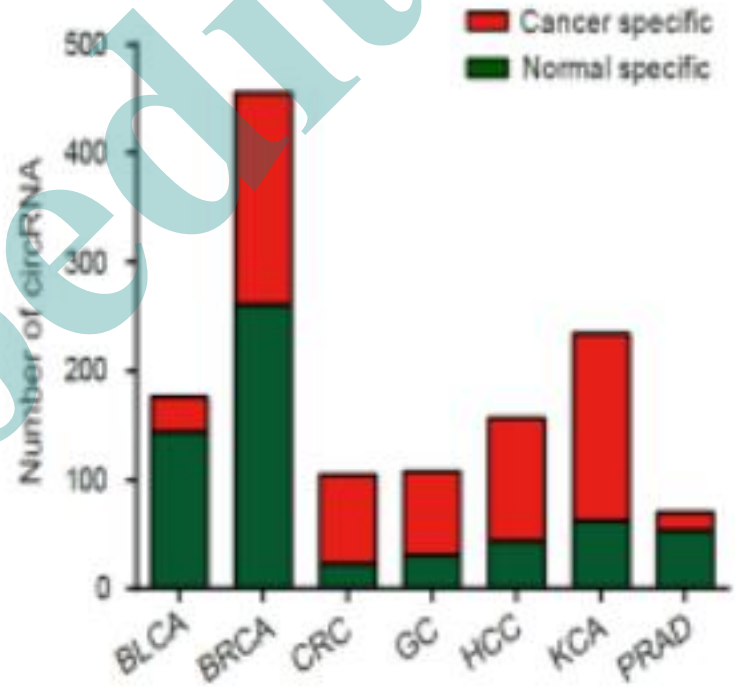
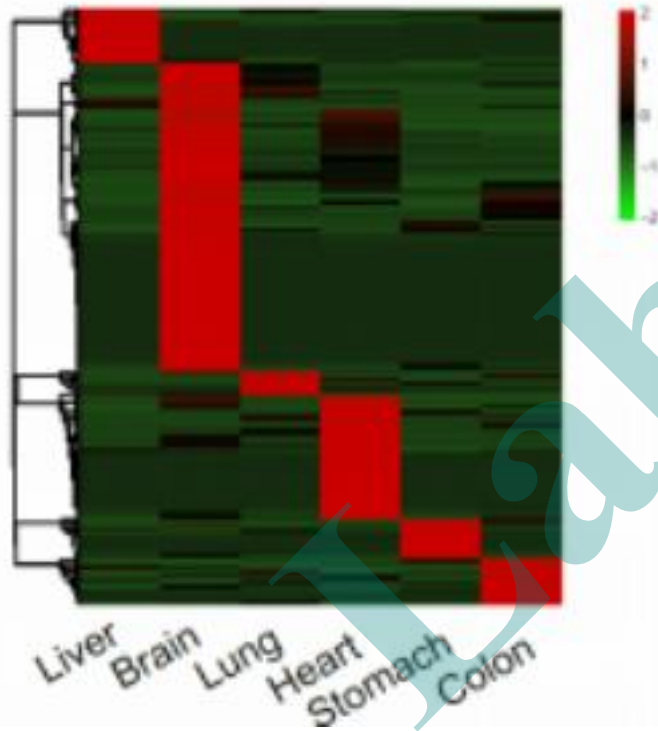


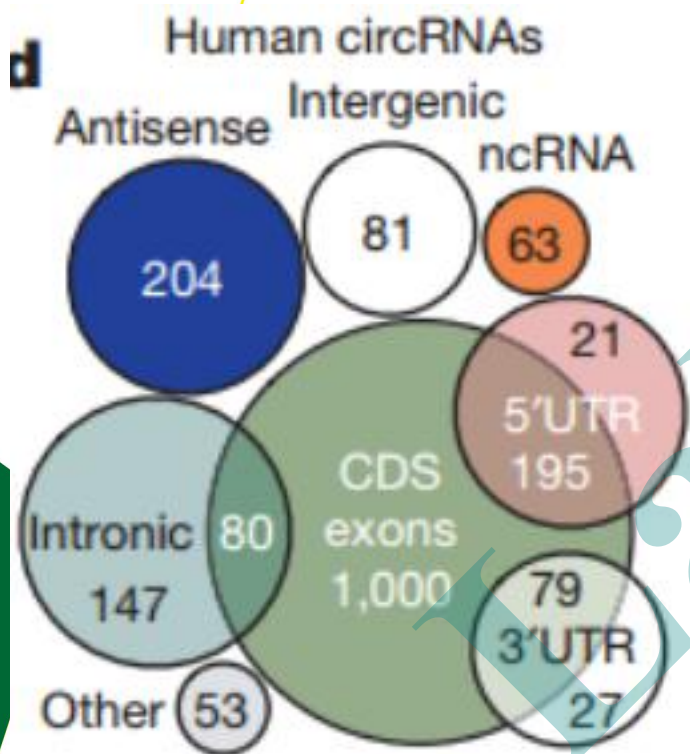
1. circRNA行使海绵功能抑制miRNA的作用；

2. circRNA能与RNA结合蛋白结合后，参与RNA转录调控；

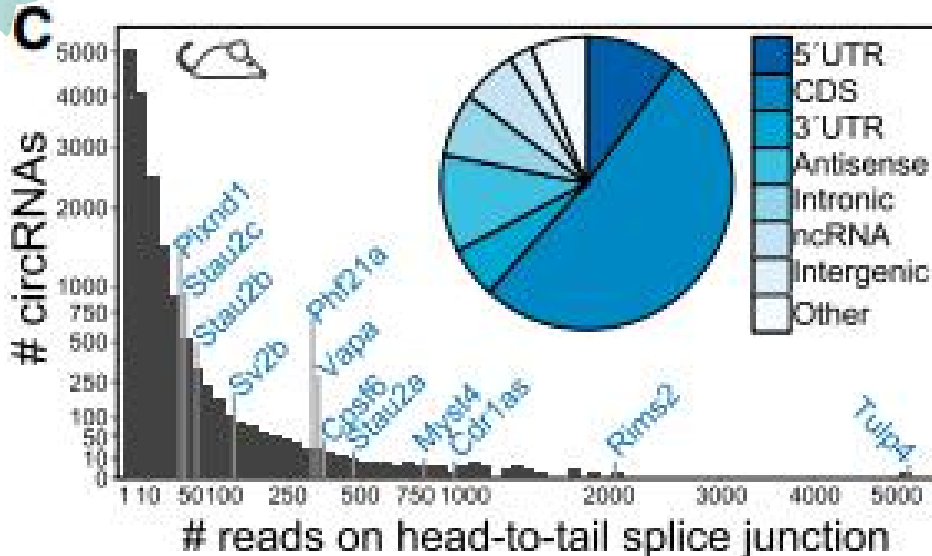
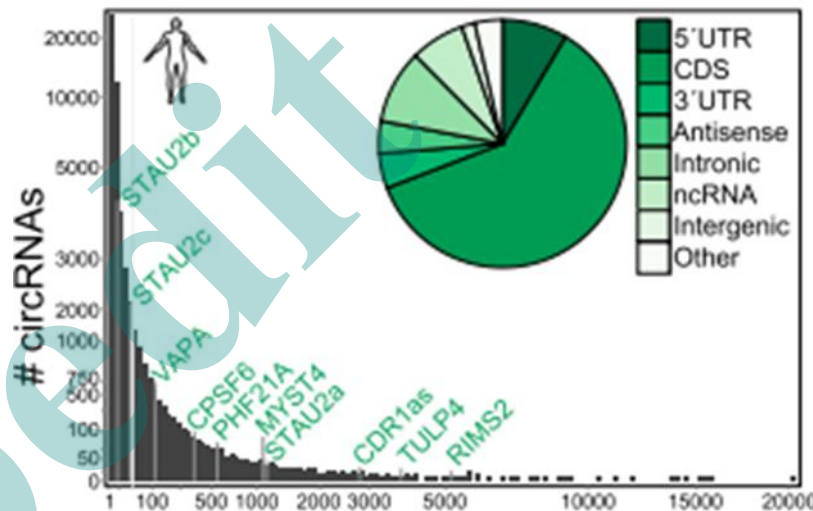
3. 某些包含内部核糖体进入位点(IRES)的circRNA能够翻译出。

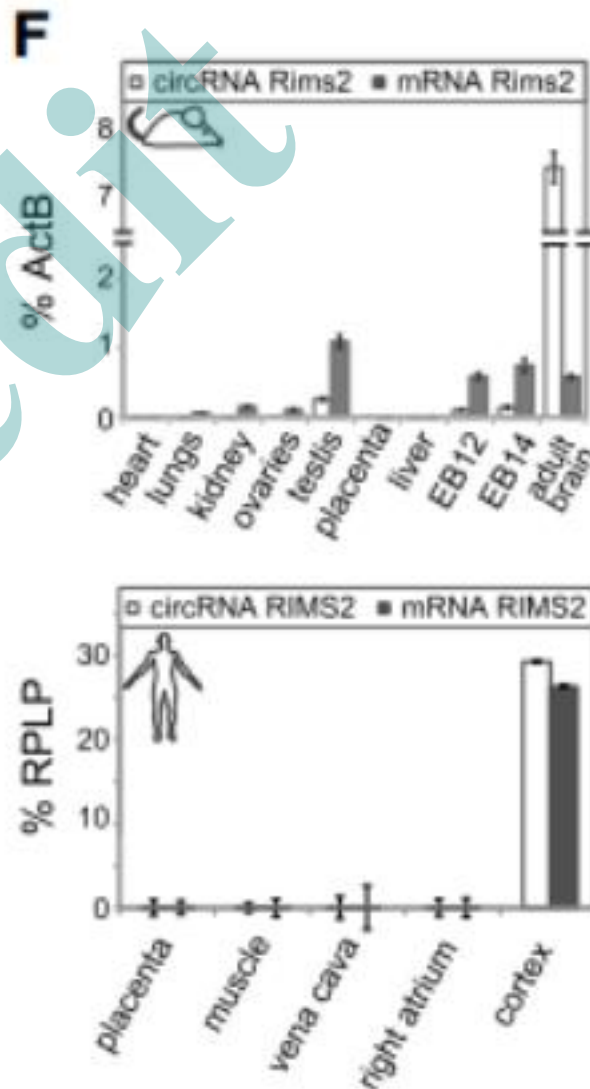
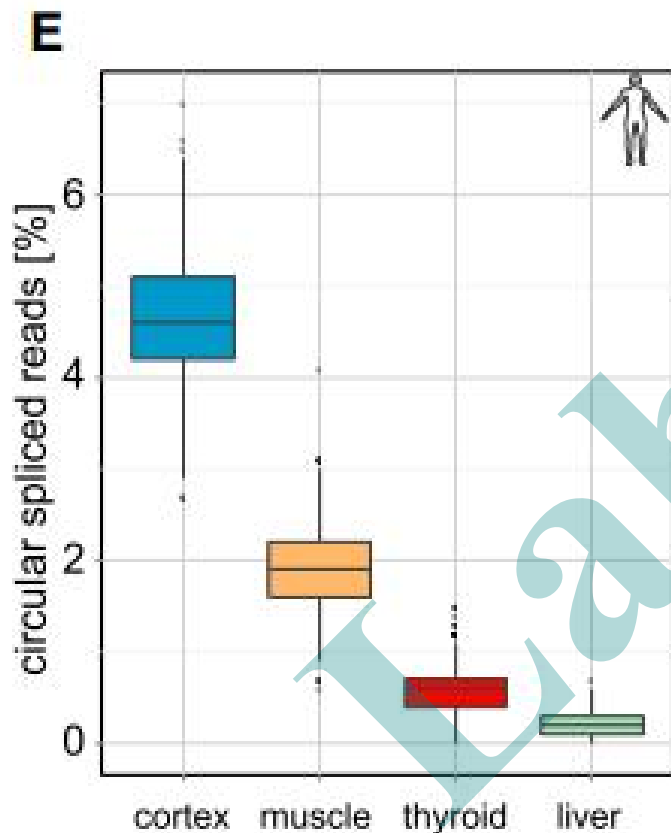
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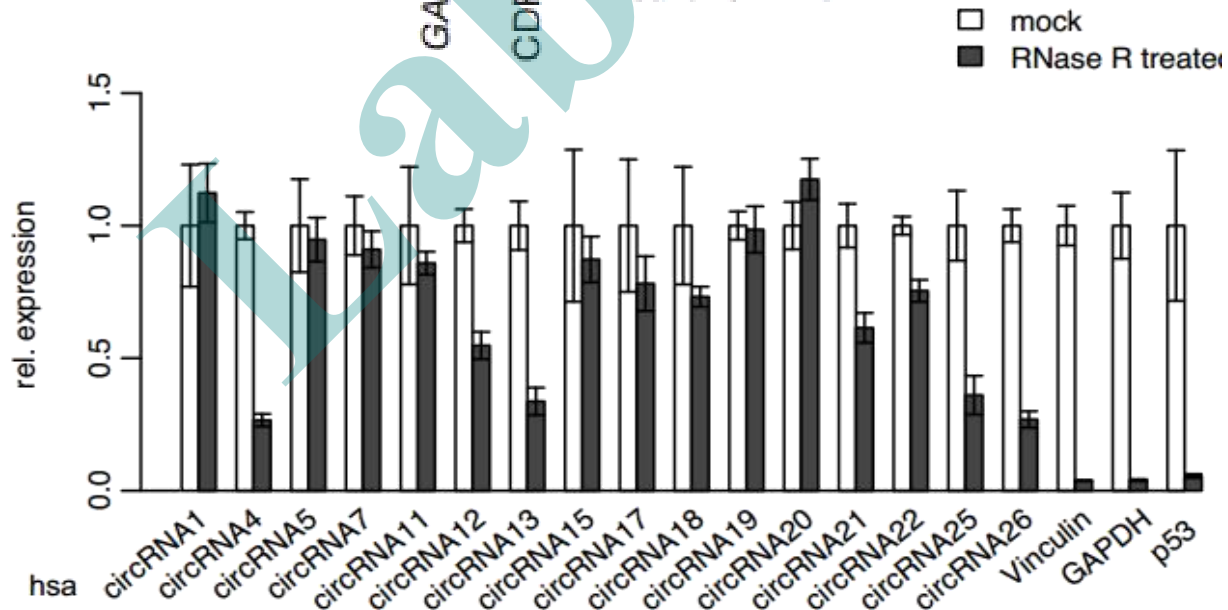
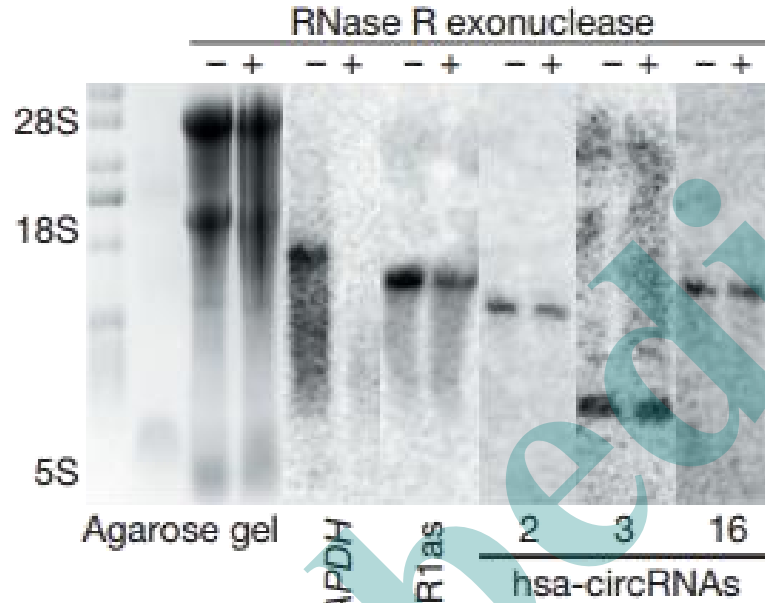


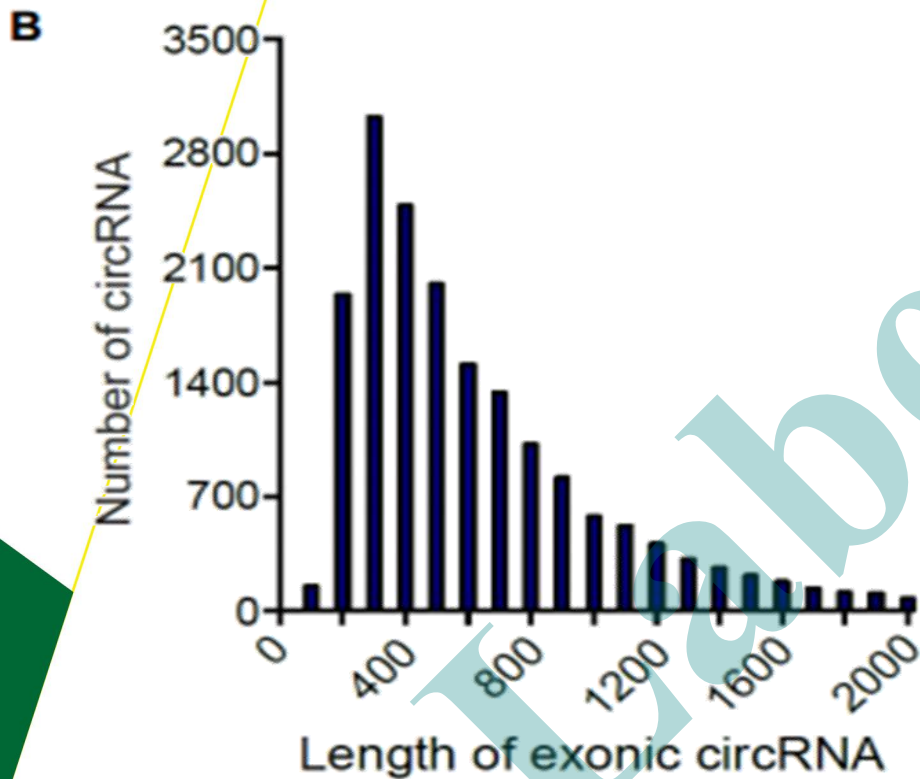
主要来源于外显子



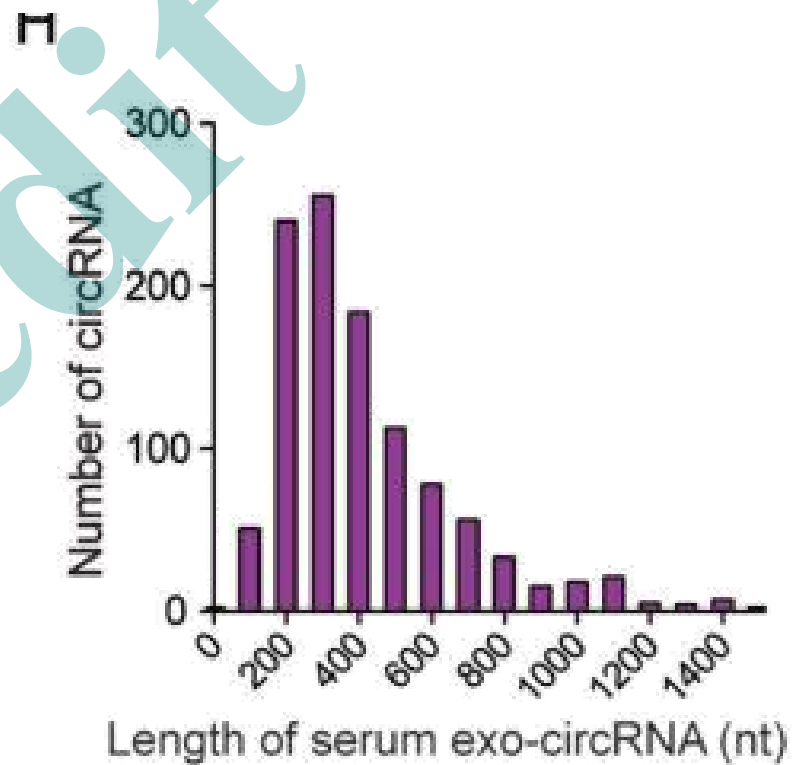


Rnase R Resistanse





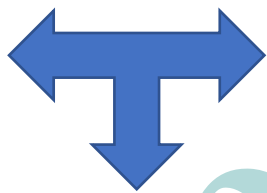
平均长度为500nt



- 一. 表达水平具有种属、组织、时间特异性
- 二. 因闭合成环不易被核酸外切酶降解
- 三. 外显子来源为主
- 四. 具有一定序列保守性
- 五. 具有可变环化
- 六. 在转录或转录后水平发挥调控作用

- 临床研究思路
- 临床+基础研究思路

1. 找差异



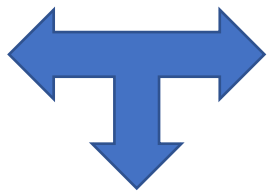
分析分子在疾病组和正常组间差异

2. 分析相关



分析与病理参数相关的相关性

3. 患者预后



表达水平与患者预后的关系

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RESEARCH ARTICLE

IF 1.521

Reduced expression of circRNA hsa_circ_0003159 in gastric cancer and its clinical significance

Mengqian Tian, Ruoyu Chen, Tianwen Li, Bingxiu Xiao

First published: 15 June 2017 [Full publication history](#)

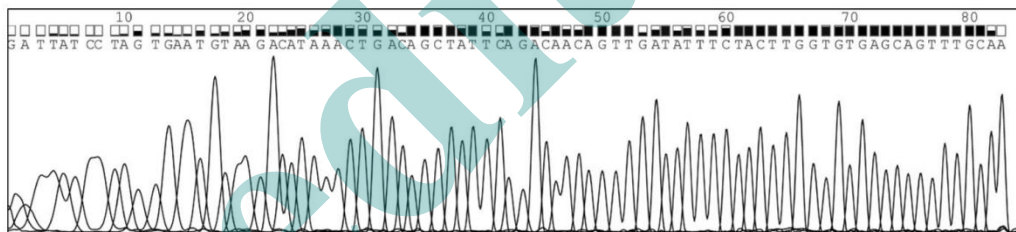
DOI: 10.1002/jcla.22281 [View/save citation](#)

主要内容:

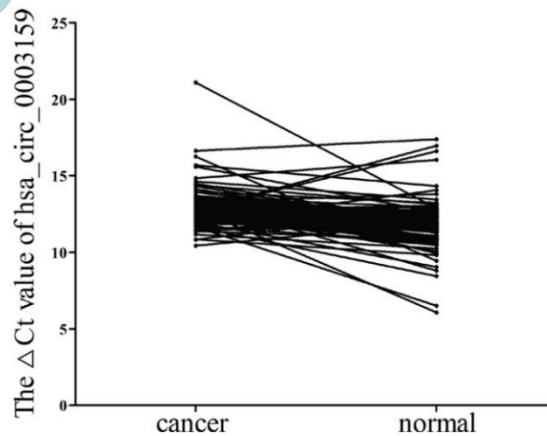
1. circRNA鉴定，并找差异；
2. 受试者工作特征曲线（ROC曲线）
3. 表达水平与临床特征相关性分析；

1. circRNA鉴定，并找差异；

设计引物并扩增，测序



癌和癌旁组织中的表达差异检测



2. 受试者工作特征曲线 (ROC曲线)

3. 表达水平与临床特征相关性分析;

Characteristics	No. of patients (%)	Mean±SD	P value
Age (y)			
<60	35 (32.4)	12.82±1.19	.657
≥60	73 (67.6)	12.94±1.38	
Gender			
Female	35 (32.4)	12.37±0.84	.003
Male	73 (67.6)	13.16±1.43	
Diameter (cm)			
<5	55 (51.9)	12.69±1.39	.095
≥5	52 (48.1)	13.12±1.22	
Differentiation			
Well	9 (8.3)	12.82±0.48	.915
Moderate	58 (53.7)	12.95±1.53	
Poor	41 (38.0)	12.85±1.10	
Lymphatic metastasis			
N0	44 (40.7)	12.79±1.11	.325
N1	22 (20.4)	13.35±1.96	
N2	8 (7.4)	12.58±1.00	
N3	34 (31.5)	12.85±1.07	
Distal metastasis			
M0	100 (92.6)	12.99±1.32	.020
M1	8 (7.4)	11.87±0.68	
Invasion			
Tis & T1	21 (19.4)	12.58±0.82	.116
T2 & T3	19 (17.6)	12.55±0.95	
T4	68 (63.0)	13.11±1.49	
TNM stage			
0 & I	30 (27.8)	12.56±0.99	.018
II & III	71 (65.7)	13.14±1.41	
IV	7 (6.5)	11.97±0.82	



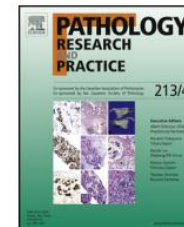
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Pathology – Research and Practice

IF 1.53

journal homepage: www.elsevier.com/locate/prp



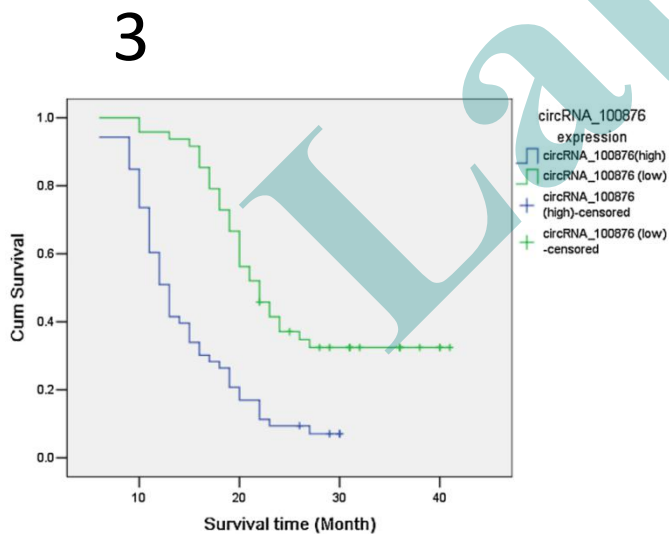
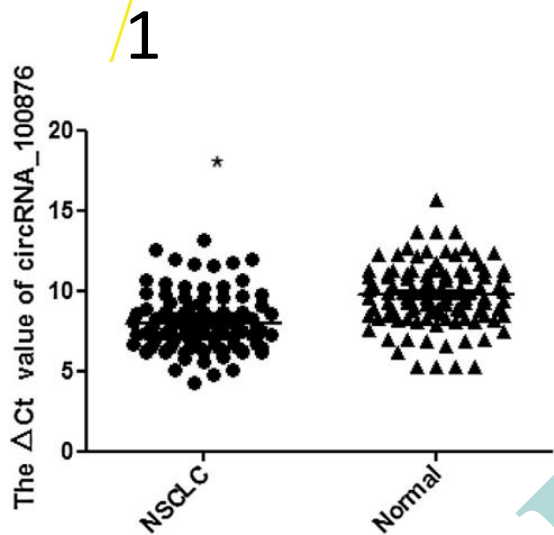
Original article

Over-expression of CircRNA_100876 in non-small cell lung cancer and its prognostic value

Jun-Tao Yao^{a,b}, Shu-Hong Zhao^c, Qiu-Ping Liu^{d,e}, Mo-Qi Lv^e, Dang-Xia Zhou^{e,g,*},
Zi-Jun Liao^f, Ke-Jun Nan^{a,**}

主要内容:

1. circRNA_100876在非小细胞肺癌组织及其癌旁组织中的差异;
2. 分析与病理参数相关的相关性;
3. 患者预后;



2

The Associations between the circRNA.100876 expression levels and clinicopathological characteristics of patients with NSCLC.

Characteristics	No. of Patients (%)	Mean \pm SD	<i>P</i> value
Age (years)			0.746
≤ 60	47(46.5%)	9.82 \pm 2.04	
>60	54(53.5%)	9.69 \pm 1.95	
Gender			0.558
Female	29(28.7%)	9.57 \pm 1.89	
Male	72(71.3%)	9.83 \pm 2.04	
Tumor diameter			0.150
≤ 5	49(48.5%)	10.05 \pm 1.98	
>5	52(51.5%)	9.48 \pm 1.98	
Pathological type			0.091
Squamous cell carcinoma	51(50.5%)	10.08 \pm 1.98	
Adenocarcinoma	50(49.5%)	9.42 \pm 1.96	
Lymphatic metastasis			0.001
Yes	33(32.7%)	8.86 \pm 1.87	
No	68(67.3%)	10.19 \pm 1.91	
Staging			0.001
I	15(14.8%)	11.57 \pm 1.84	
II	43(42.6%)	9.82 \pm 1.76	
IV	43(42.6%)	9.06 \pm 1.88	
Tumor differentiation			0.105
well	6(5.9%)	11.21 \pm 2.74	
moderate	64(63.4%)	9.82 \pm 1.83	
poor	31(30.7%)	9.35 \pm 2.09	

* *P* < 0.05, compared among different groups.



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Clinica Chimica Acta

IF 2.87

journal homepage: www.elsevier.com/locate/clinchim

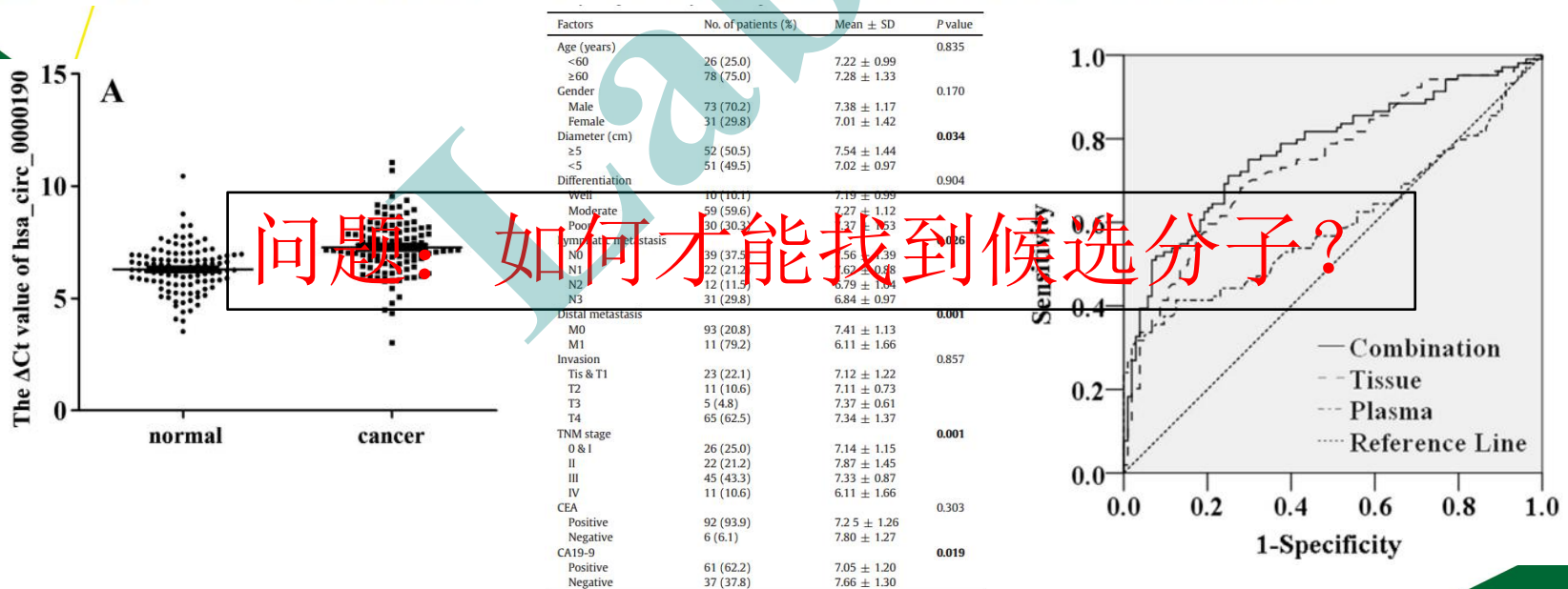


Using circular RNA hsa_circ_0000190 as a new biomarker in the diagnosis of gastric cancer[☆]



Shijun Chen, Tianwen Li, Qianfu Zhao, Bingxiu Xiao, Junming Guo *

Department of Biochemistry and Molecular Biology, Zhejiang Key Laboratory of Pathophysiology, Ningbo University School of Medicine, Ningbo 315211, China





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BioMed Research International

Impact Factor 2.476

Research Article

Microarray Analysis of Circular RNA Expression Profile Associated with 5-Fluorouracil-Based Chemoradiation Resistance in Colorectal Cancer Cells

Wei Xiong,¹ Yi-Qin Ai,¹ Yun-Fen Li,¹ Qing Ye,² Zheng-Ting Chen,¹ Ji-Yong Qin,¹ Qiu-Yan Liu,¹ Hong Wang,¹ Yun-He Ju,¹ Wen-Hui Li,¹ and Yun-Feng Li³

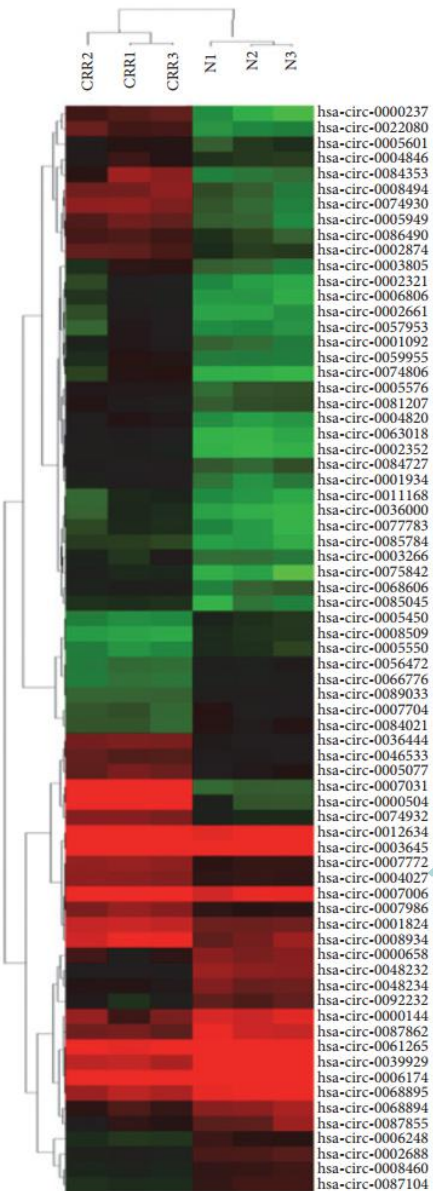
研究内容:

1. 芯片检测circRNA
2. 数据分析
3. 稍加验证

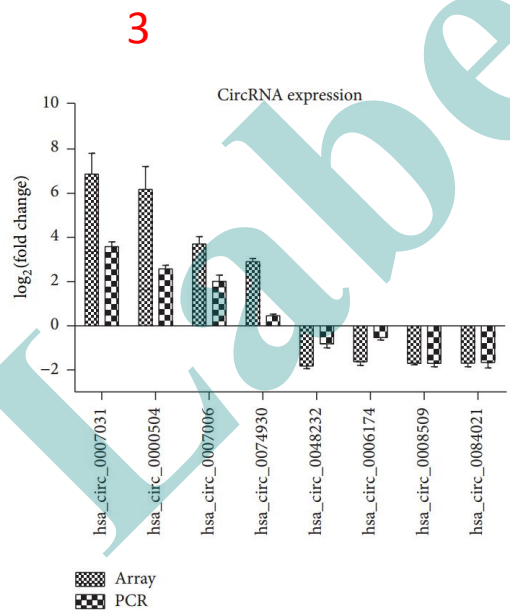
TABLE 2: Top modulated circRNAs in chemoradiation-resistant colorectal cancer.

circRNA	Gene symbol	Chrom	Regulation	p value	FC (abs)
hsa_circ_0007031	TUBGCP3	chr13	Up	2.29E - 04	116.6
hsa_circ_0000504	TUBGCP3	chr13	Up	6.96E - 04	74.4
hsa_circ_0007006	DYM	chr18	Up	7.58E - 05	13
hsa_circ_0000237	HNRNPF	chr10	Up	2.26E - 04	8.7
hsa_circ_0074930	SLIT3	chr5	Up	8.33E - 05	7.6
hsa_circ_0084353	PRKDC	chr8	Up	3.61E - 03	6.8
hsa_circ_0022080	NUP160	chr11	Up	6.79E - 05	6.2
hsa_circ_0008494	ARIDIA	chr1	Up	1.82E - 04	6.2
hsa_circ_0005949	ZNF608	chr5	Up	2.73E - 04	5.6
hsa_circ_0002874	CLINT1	chr5	Up	5.74E - 03	4.5
hsa_circ_0003805	hsa_circ_0048232	chr19	Down	1.76E - 05	3.3
hsa_circ_0002321	hsa_circ_0006806	chr9	Down	5.28E - 04	2.7
hsa_circ_0006611	hsa_circ_0008509	chr12	Down	2.84E - 05	2.6
hsa_circ_0057953	hsa_circ_0001092	chr8	Down	3.80E - 04	2.6
hsa_circ_0059955	hsa_circ_0074806	chr9	Down	1.49E - 03	2.6
hsa_circ_0074806	hsa_circ_0005576				
hsa_circ_0005576	hsa_circ_0081207				
hsa_circ_0081207	hsa_circ_0004820				
hsa_circ_0004820	hsa_circ_0063018				
hsa_circ_0063018	hsa_circ_0002352				
hsa_circ_0002352	hsa_circ_0084727				
hsa_circ_0084727	hsa_circ_0001934				
hsa_circ_0001934	hsa_circ_0011168				
hsa_circ_0011168	hsa_circ_0036000				
hsa_circ_0036000	hsa_circ_0077783				
hsa_circ_0077783	hsa_circ_0085784				
hsa_circ_0085784	hsa_circ_0003266				
hsa_circ_0003266	hsa_circ_0075842				
hsa_circ_0075842	hsa_circ_0068606				
hsa_circ_0068606	hsa_circ_0085045				
hsa_circ_0085045	hsa_circ_0005450				
hsa_circ_0005450	hsa_circ_0008509				
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hsa_circ_0006174	hsa_circ_0068895				
hsa_circ_0068895	hsa_circ_0068894				
hsa_circ_0068894	hsa_circ_0087855				
hsa_circ_0087855	hsa_circ_0006248				
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hsa_circ_0008460	hsa_circ_0087104				

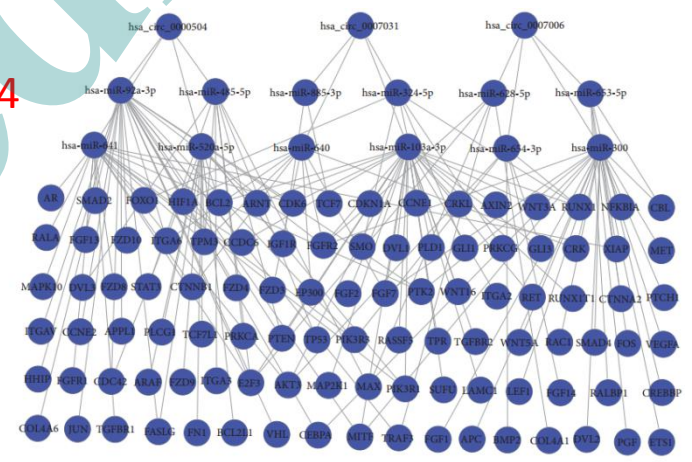
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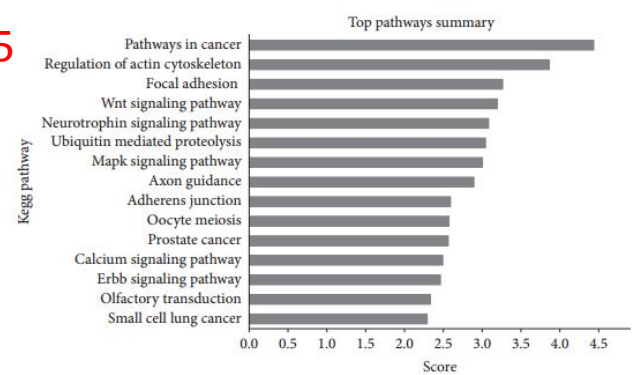
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4



5



International Journal
of Molecular
Medicine

IF 2.34

Altered expression profiles of circular RNA in colorectal cancer tissues from patients with lung metastasis

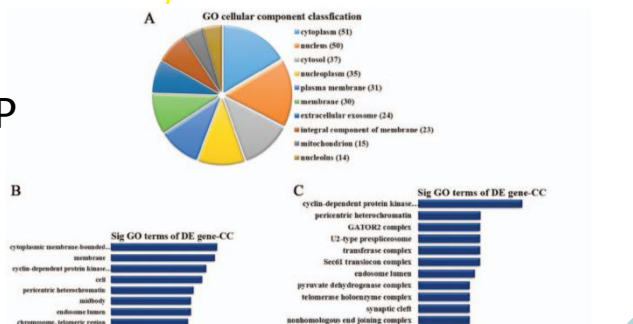
YUJIAN ZENG^{1,2*}, YU XU^{1,2*}, RUO SHU^{1,3}, LIANG SUN^{2,3}, YAN TIAN^{2,3}, CHENGMIN SHI^{2,3},
ZHIBIN ZHENG^{1,3}, KUNHUA WANG¹⁻³ and HUAYOU LUO¹⁻³

研究内容:

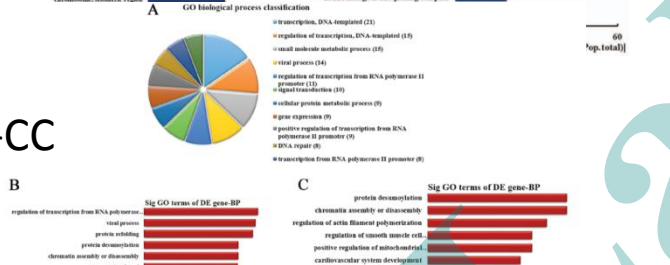
1. 芯片检测circRNA
2. 数据分析

1. 芯片检测，并分析circRNA来源，筛选top10上调/下调的circRNA

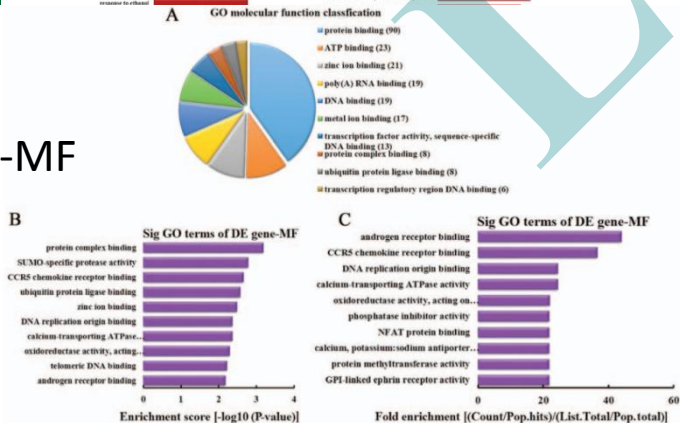
GO-BP



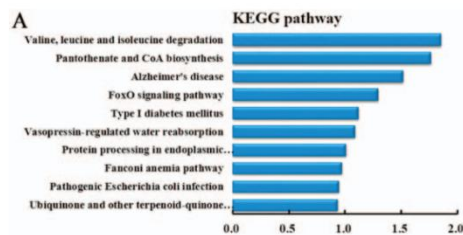
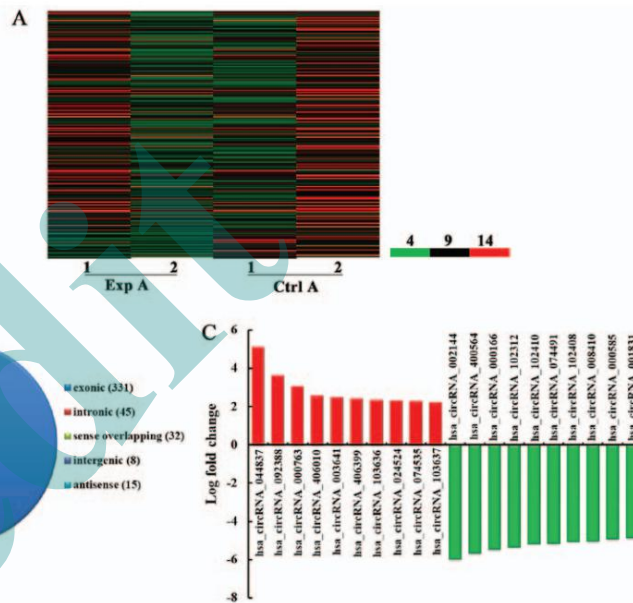
GO-CC



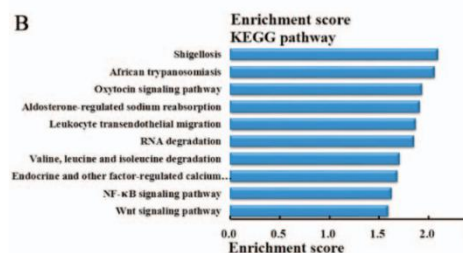
GO-MF



2. GO分析



3. KEGG



hsa_circ_0013958: a circular RNA and potential novel biomarker for lung adenocarcinoma

Xiaoli Zhu^{1,2,#}, Xiyong Wang^{1,2,#}, Shuzhen Wei¹, Yan Chen², Yang Chen², Xiaobo Fan², Shuhua Han¹ and Guoqiu Wu^{2,3}

1 Department of Respiratory, Zhongda Hospital, Southeast University, Nanjing, China

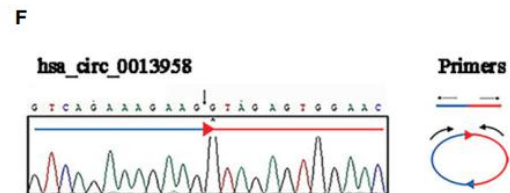
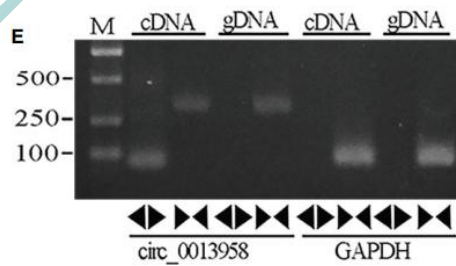
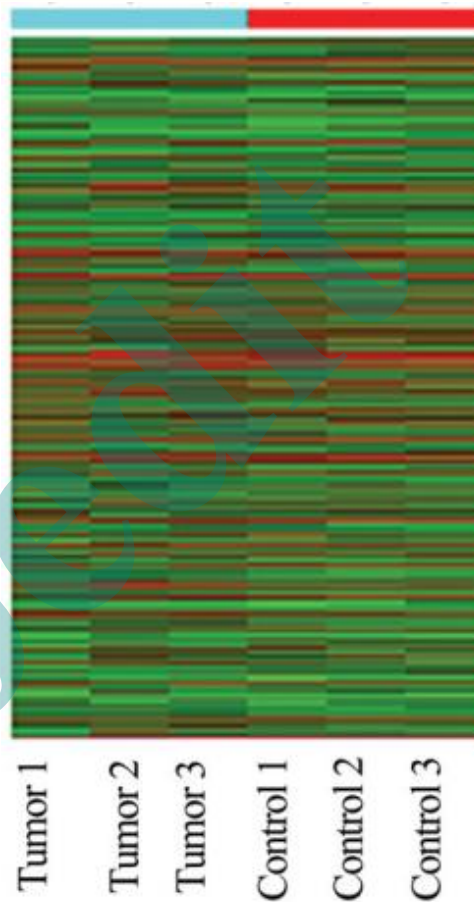
2 Medical School of Southeast University, Nanjing, China

3 Center of Clinical Laboratory Medicine, Zhongda Hospital, Southeast University, Nanjing, China

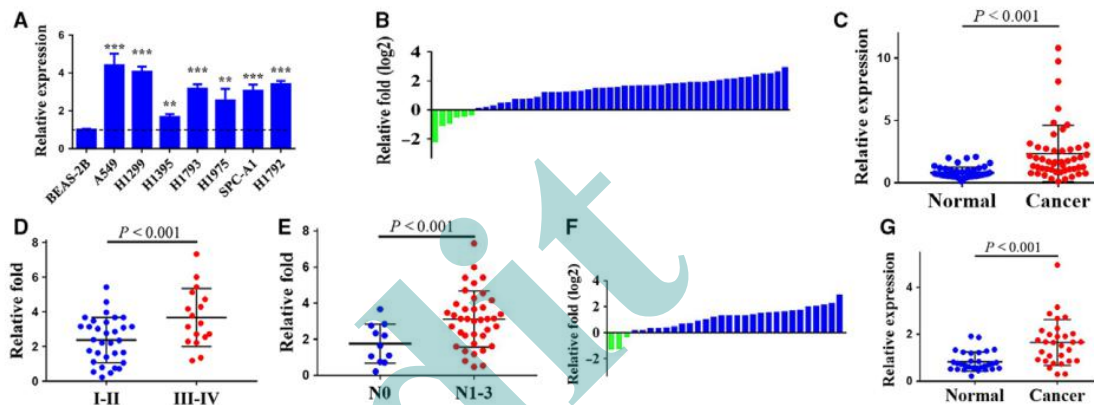
研究思路:

1. 芯片筛选, circRNA筛选, 并进行一般鉴定;
2. 临床样本验证表达水平差异, 分析相关性;
3. 受试者工作特征曲线 (ROC曲线)
4. 表达水平与临床特征相关性分析;
5. 功能获得验证 (细胞实验)
6. 与miRNA互作 (细胞)

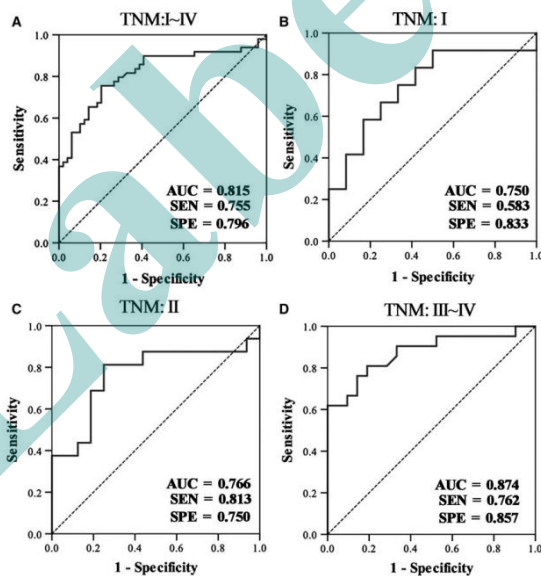
1. 筛选circRNA及鉴定



2. 组织及细胞水平验证差异性

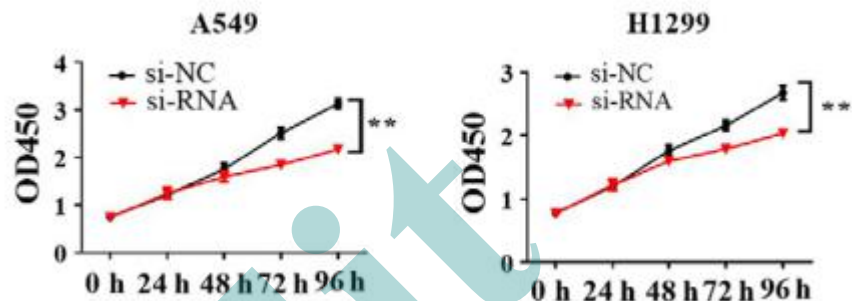


3. ROC曲线分析及患者特征相关性分析

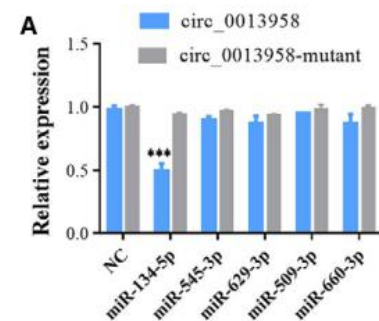
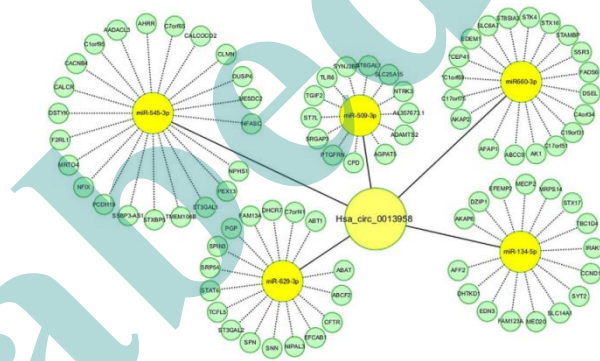


hsa_circ_0013958			
Characteristics	Low-level (no. 10)	High-level (no. 39)	P value
Sex			0.931
Male	6	24	
Female	4	15	
Age (years)			0.723
≥ 60	5	22	
< 60	5	17	
Smoking			0.588
Yes	4	12	
No	6	27	
Lymphatic metastasis			0.006*
N0	5	6	
N1	4	13	
N2	1	18	
N3	0	2	
Diameter (mm)			0.076
3	7	15	
3	3	24	
TNM stage			0.009*
I	5	7	
II	4	12	
III-IV	1	20	
Differentiation			0.474
Poor	1	6	
Moderate	2	11	
Well	7	22	

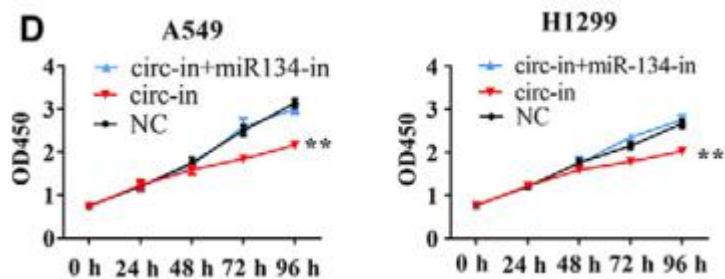
4. siRNA-circRNA功能验证

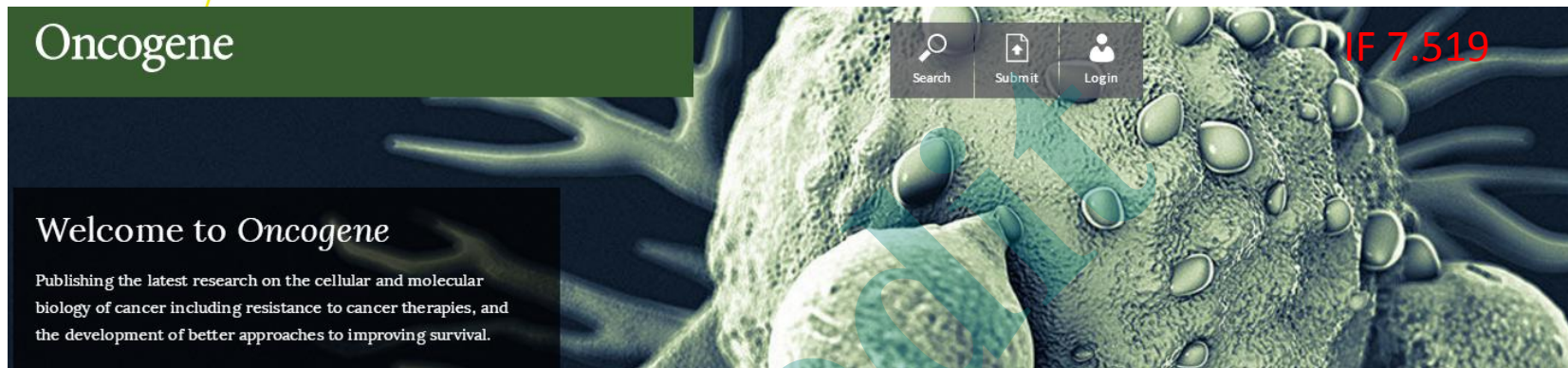


5. 数据挖掘筛选互作miRNA及验证



6. 功能验证





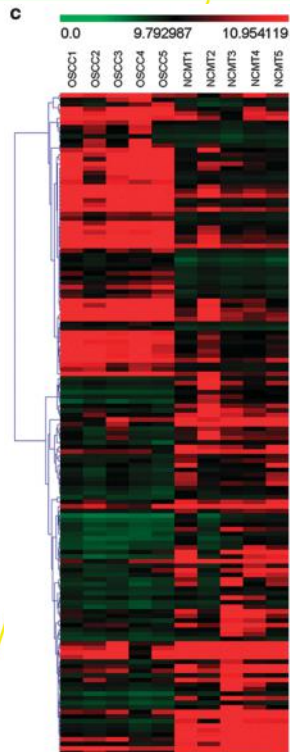
ORIGINAL ARTICLE

circRNA_100290 plays a role in oral cancer by functioning as a sponge of the miR-29 family

L Chen¹, S Zhang¹, J Wu², J Cui³, L Zhong¹, L Zeng¹ and S Ge¹

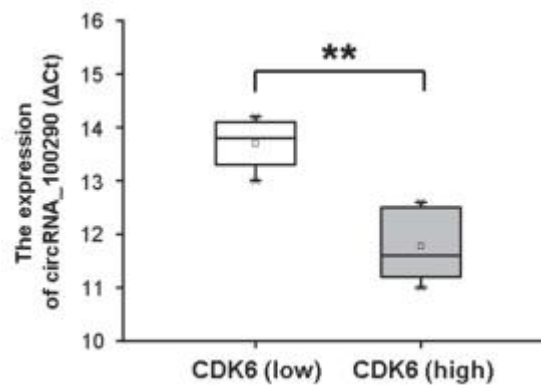
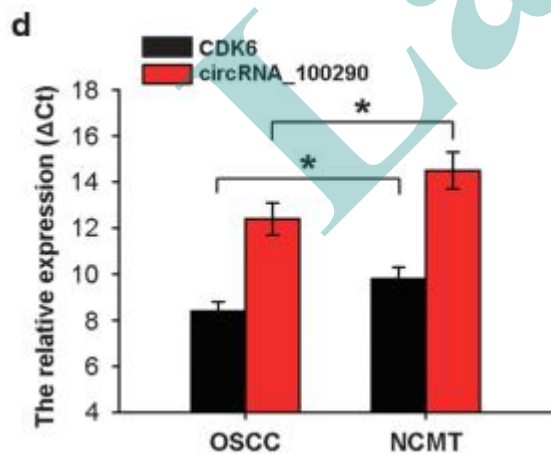
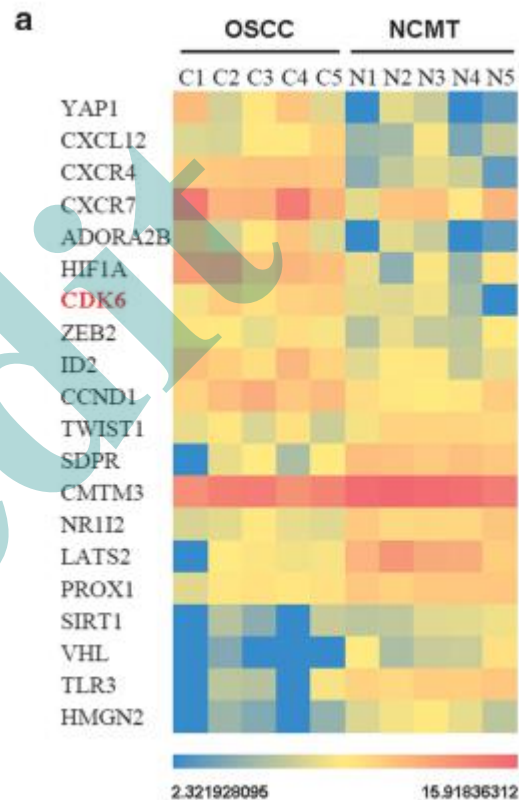
研究内容:

1. 芯片筛选目的circRNA和mRNA，并验证；
2. circRNA及其母基因功能缺失验证；
3. circRNA-miRNA-mRNA互作

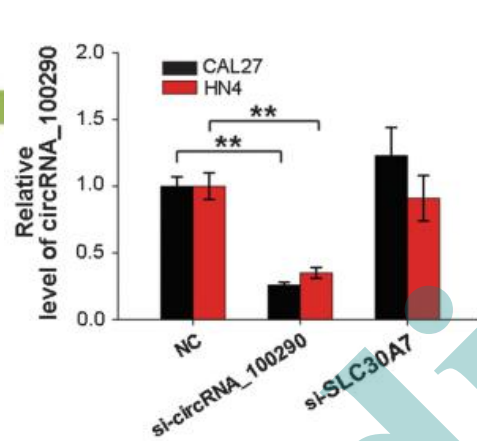
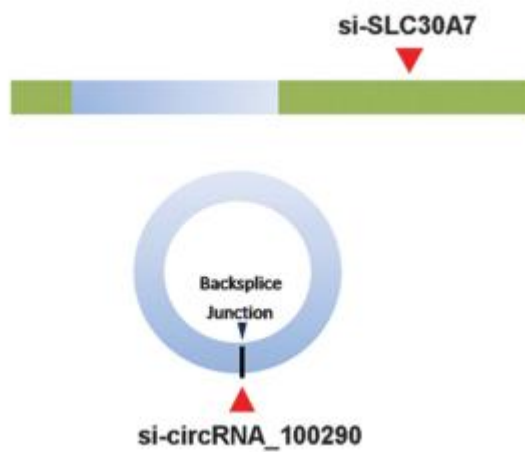


d

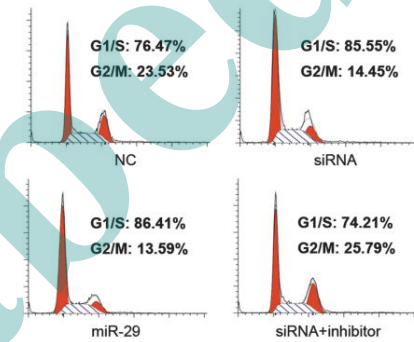
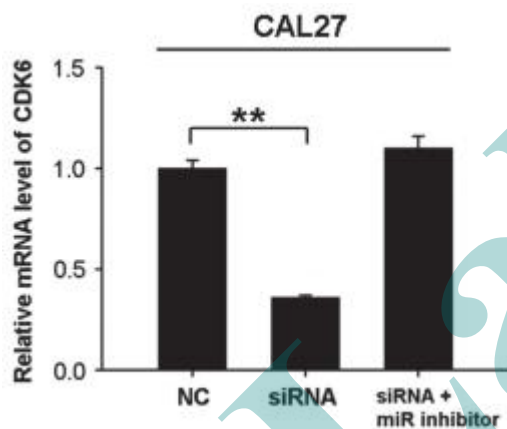
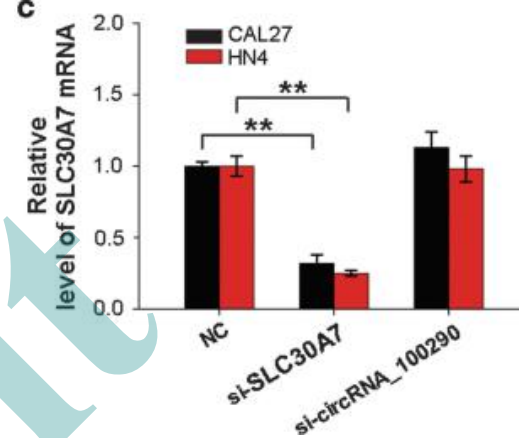
circRNA ID	Gene symbol	Fold changes	P-value
circRNA_100291	SLC30A7	7.2920687	2.6311E-05
→ circRNA_100290	SLC30A7	6.9112928	1.1097E-05
circRNA_104357	DBNL	4.9560191	1.3006E-04
circRNA_101308	TMCO3	4.7585811	1.07998E-03
circRNA_102069	NT5C3L	4.0608436	2.2482E-05
circRNA_000671	SEC14L6	3.9940817	9.1985E-06
circRNA_102990	SLC23A2	3.9834283	2.5487E-04
circRNA_103262	TBC1D22A	3.7544461	2.7082E-04
circRNA_101407	NEK9	3.7496458	2.9714E-04
circRNA_104515	AGK	3.7415432	1.5707E-04
circRNA_100928	PICALM	-8.8651961	1.5507E-05
circRNA_100214	STIL	-7.9215383	1.4271E-03
circRNA_104233	SCAF8	-7.635695	2.9062E-04
circRNA_102926	CUL3	-6.9144825	1.87796E-05
circRNA_001207	RFX3	-6.8248789	1.6413E-03
circRNA_104081	LINC00340	-6.3268287	6.0206E-05
circRNA_001309	PHYKPL	-6.1952783	2.6429E-03
circRNA_000618	FAM65A	-6.1939142	7.214E-06
circRNA_400029	RPL13	-6.1774341	3.1039E-05
circRNA_400101	RPL7A	-5.721857	3.5035E-05



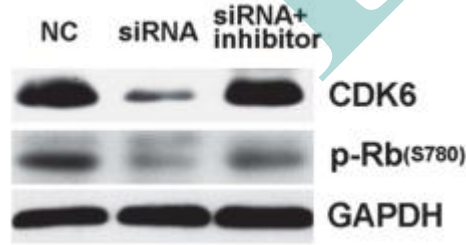
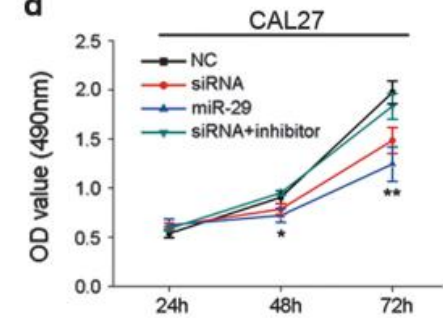
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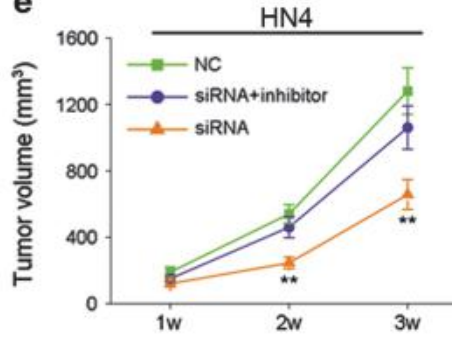
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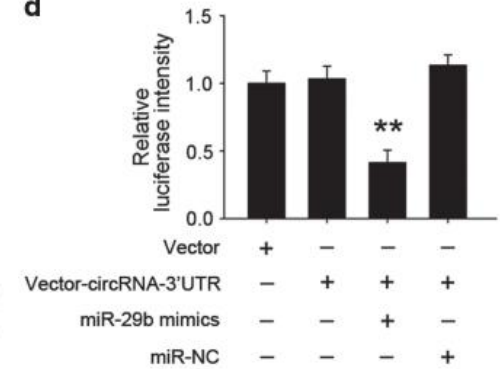
d



e



d



Oncotarget



ONLINE ISSN: 1949-2553

www.impactjournals.com/oncotarget/

Oncotarget, 2017, Vol. 8, (No. 37), pp: 61687-61697

Research Paper

Increased circular RNA UBAP2 acts as a sponge of miR-143 to promote osteosarcoma progression

Hao Zhang^{1,*}, Guangchao Wang^{1,*}, Chen Ding^{1,*}, Peng Liu^{2,*}, Renkai Wang¹, Wenbin Ding¹, Dake Tong¹, Dajiang Wu¹, Cheng Li¹, Qiang Wei¹, Xin Zhang¹, Di Li¹, Peizhao Liu¹, Haochen Cui¹, Hao Tang¹ and Fang Ji¹

研究内容:

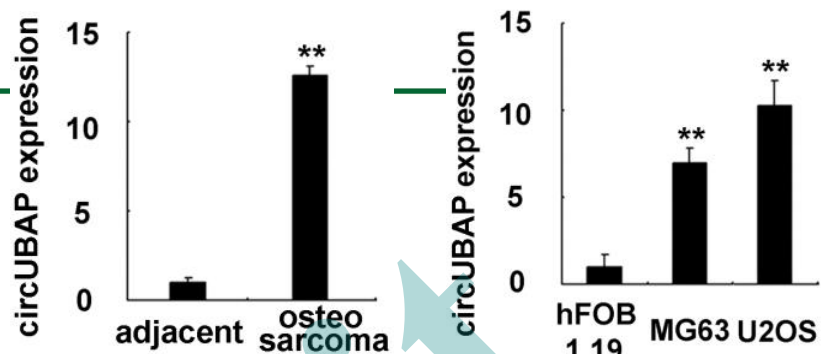
临床

1. circRNA_UBAP2在癌及癌旁组织中的表达差异;
2. circRNA表达水平与肿瘤分期和总生存的相关性;

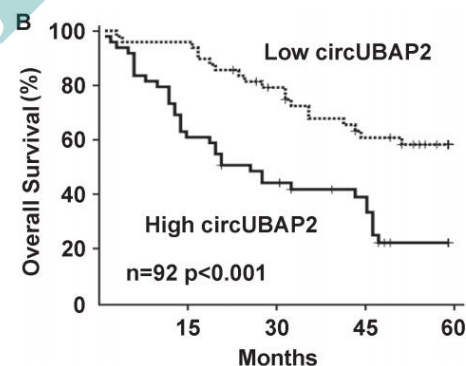
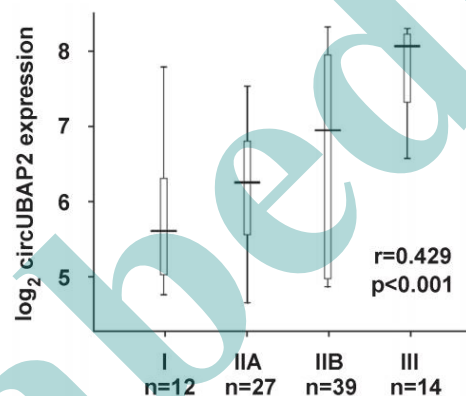
基础

3. 对circRNA进行过表达和敲低, 进行功能验证;
4. RIP筛选miRNA
5. 共表达验证

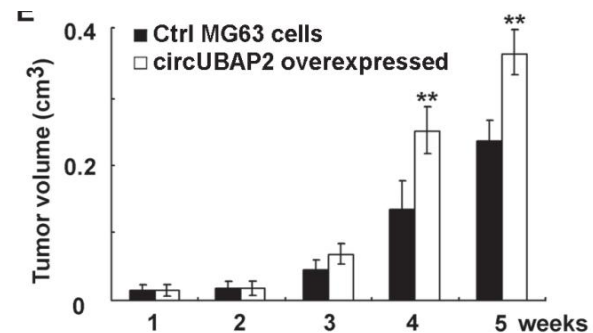
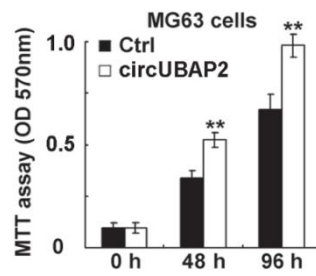
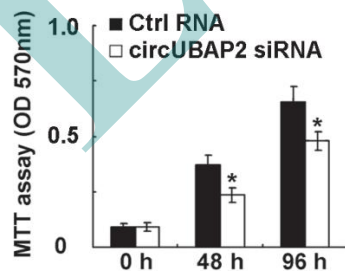
1. 检测差异



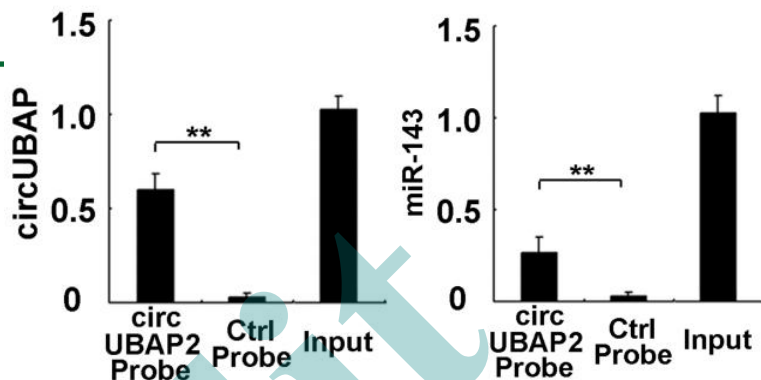
2. 分析相关性



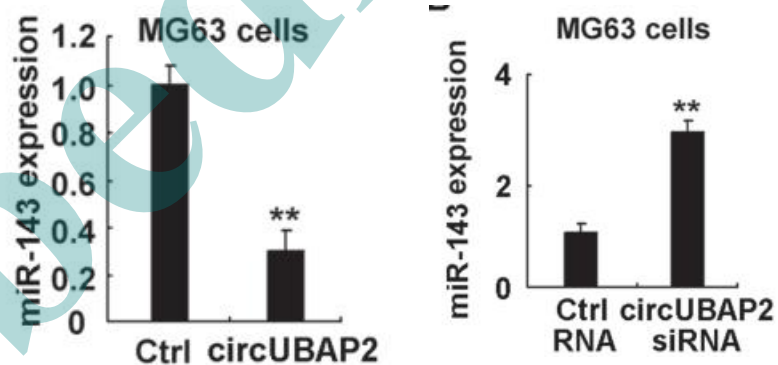
3. 验证功能



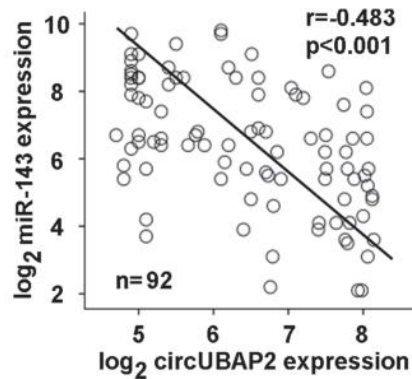
4. RIP筛选miRNA

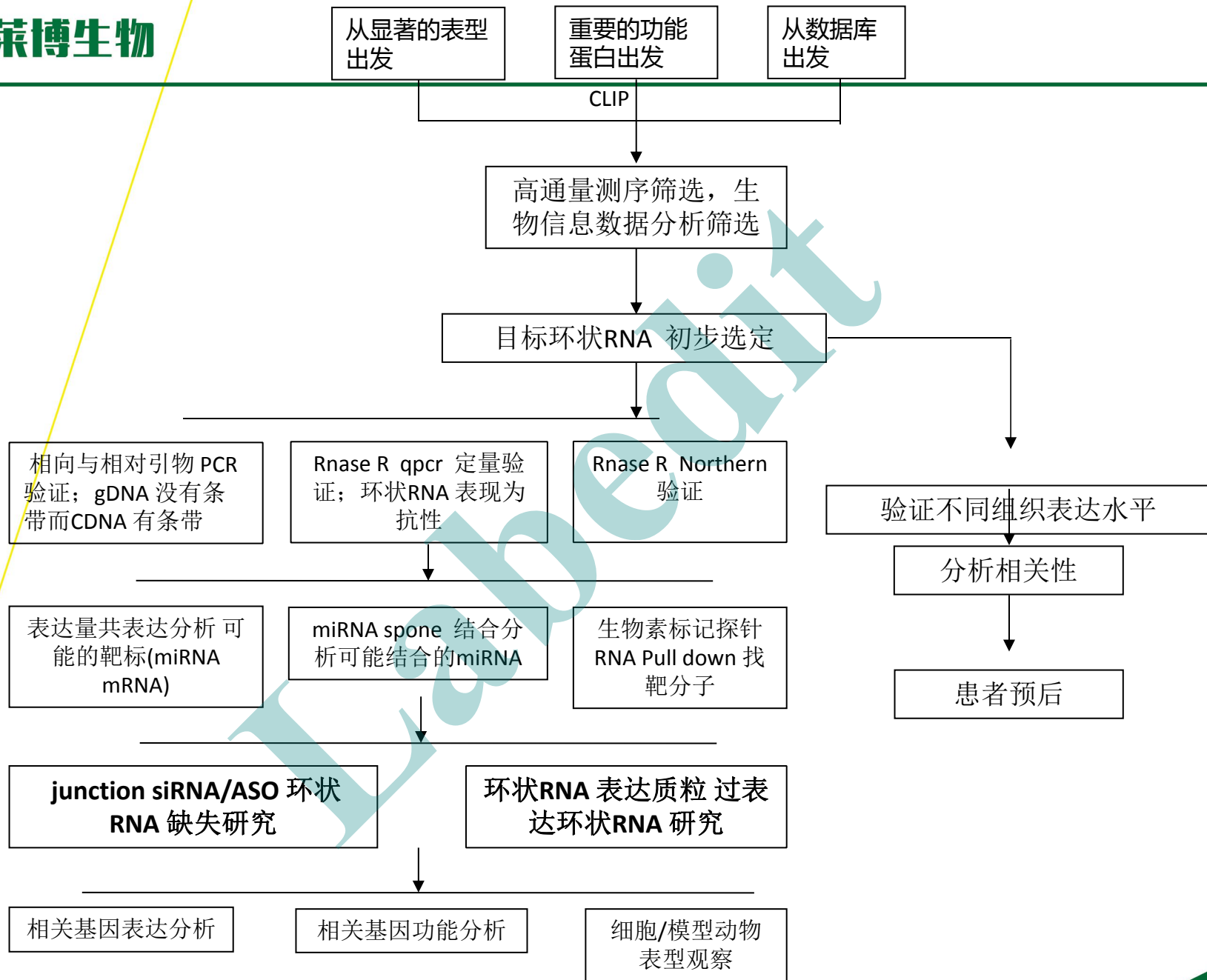


5. 验证两者共表达情况



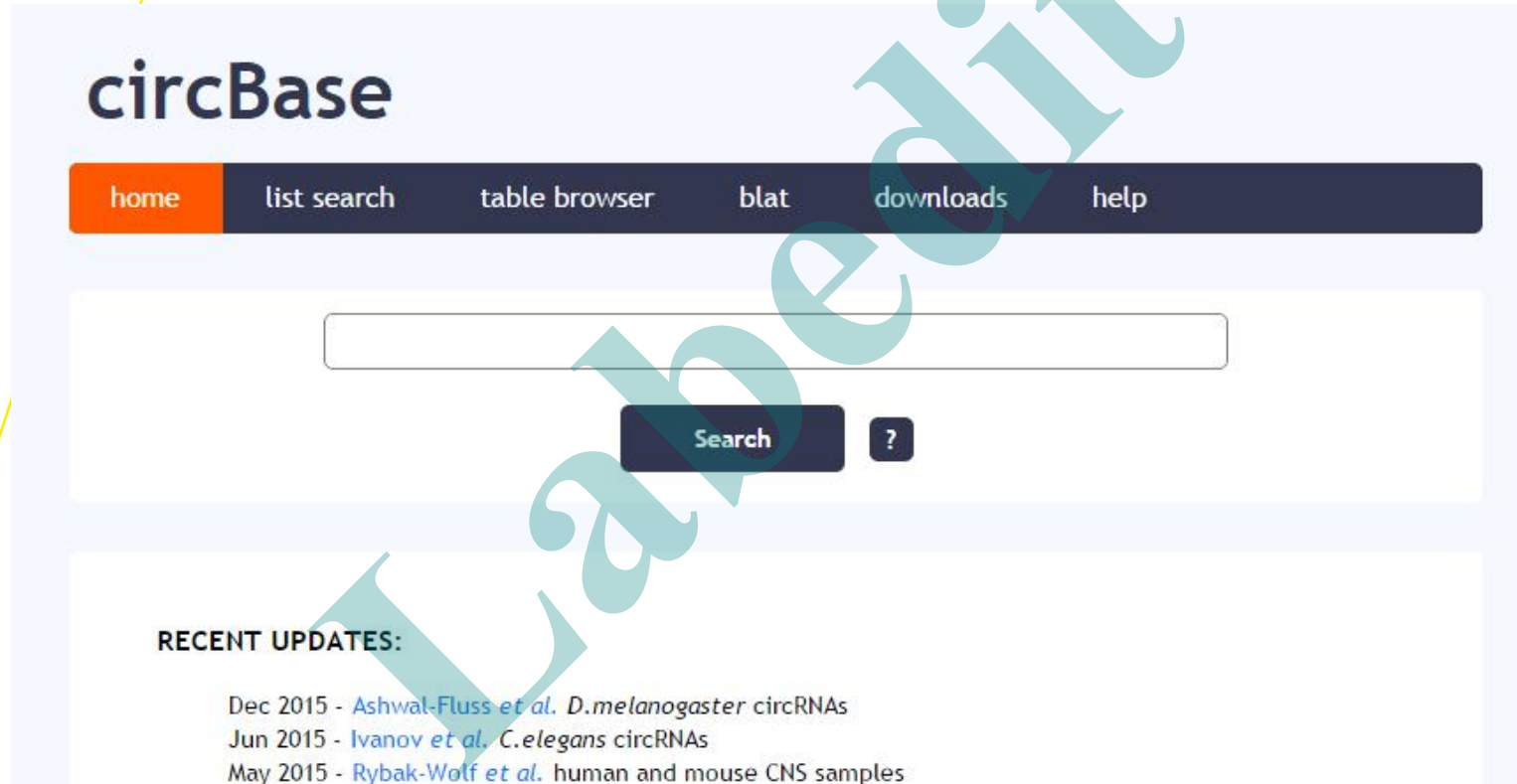
6. 在组织中验证两者相关性





1. circBase: <http://www.circbase.org/>
2. circNET: <http://circnet.mbc.nctu.edu.tw/>
3. StarBase V2: <http://deepbase.sysu.edu.cn/>
4. CircInteractome: <http://circinteractome.nia.nih.gov/>
5. Circ2Traits: <http://gyanxet-beta.com/circdb/>
6. CSCD: <http://gb.whu.edu.cn/CSCD>
7. exoRBase: <http://www.exoRBase.org>

<http://www.circbase.org/>



The screenshot shows the circBase website interface. At the top, the title "circBase" is displayed in a large, dark blue font. Below the title is a dark blue navigation bar with several menu items: "home" (highlighted in orange), "list search", "table browser", "blat", "downloads", and "help". In the center of the page, there is a large, empty white search input field. Below the search field is a dark blue "Search" button and a small square button with a question mark. At the bottom of the page, there is a section titled "RECENT UPDATES:" followed by three entries: "Dec 2015 - [Ashwal-Fluss et al.](#) *D.melanogaster* circRNAs", "Jun 2015 - [Ivanov et al.](#) *C.elegans* circRNAs", and "May 2015 - [Rybak-Wolf et al.](#) human and mouse CNS samples". A large, light blue watermark reading "Lanedit" is overlaid diagonally across the entire page.

基于转录组测序的数据建立的数据库

<http://circnet.mbc.nctu.edu.tw/>

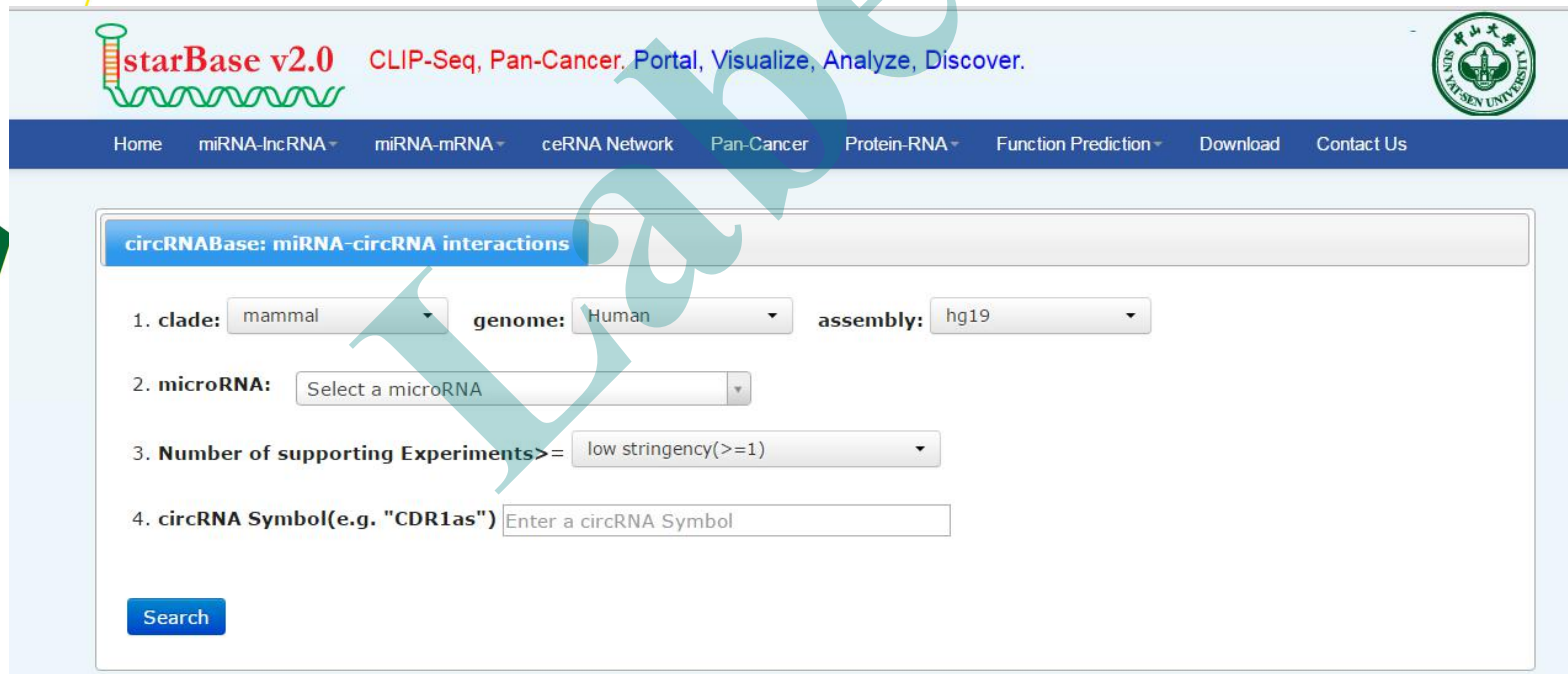
The screenshot displays the CircNet web application interface. The top navigation bar includes 'SEARCH', 'TUTORIAL', 'BLAST', 'CHANGELOG', 'CONTACT US', and 'DOWNLOAD'. Below the navigation bar, there are search fields for 'Search Gene' and 'Search MiRNA'. The main content area is divided into two panels. The left panel shows a network diagram with 'ZEB1' at the center, connected to various miRNAs and circRNAs. The right panel shows a heatmap of expression data (FPKM) for several circRNAs across 13 samples. Below the heatmap is a JBrowse genomic browser showing the reference sequence and various genomic features like repeats and duplications.

Expression Heatmap Data (FPKM):

ID	1	2	3	4	5	6	7	8	9	10	11	12	13
hsa-circ-ZEB1-antisense.16	Low	Low	Low	Low	Low	Low	Low	Low	Low	High	Low	Low	Low
hsa-circ-ZEB1-antisense.18	High	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
hsa-circ-ZEB1-antisense.2	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
hsa-circ-ZEB1-antisense.4	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
hsa-circ-ZEB1-overlap.14	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
hsa-circ-ZEB1-overlap.2	High	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
hsa-circ-ZEB1-overlap.3	High	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low

A platform for annotating and discovering small and long ncRNAs (microRNAs, siRNAs, piRNAs...) from next generation sequencing data

<http://deepbase.sysu.edu.cn/>



starBase v2.0 CLIP-Seq, Pan-Cancer, Portal, Visualize, Analyze, Discover.

Home miRNA-lncRNA miRNA-mRNA ceRNA Network Pan-Cancer Protein-RNA Function Prediction Download Contact Us

circRNABase: miRNA-circRNA interactions

1. **clade:** mammal **genome:** Human **assembly:** hg19

2. **microRNA:** Select a microRNA

3. **Number of supporting Experiments** >= low stringency(>=1)

4. **circRNA Symbol**(e.g. "CDR1as") Enter a circRNA Symbol

Search

<http://circinteractome.nia.nih.gov/>



Circular RNA Interactome



Home

Circular RNA

RBP on CircRNA

miRNA Target Sites

Divergent Primers

siRNA Design

Help

Welcome to Circular RNA Interactome

Hundreds of RNA-binding proteins and miRNAs has been shown to regulate gene expression in mammals. Recently, circular RNAs (circRNAs) have been reported to regulate gene expression by sponging miRNA. Here we have used 109 datasets of RNA-binding proteins (RBPs) and queried circRNAs (Glažar et al. 2014) for RNA-binding sites. CircInteractome predicts the miRNAs which can potentially target the circRNAs using the Targetscan prediction tool (Grimson et al., 2007). This computational tool enables the prediction and mapping of binding sites for RBPs and miRNAs on reported circRNAs.

Highlights of CircInteractome:

- Searches circRNAs name
- Searches the genomic position and best-matching transcripts of the circRNA
- Retrieves genomic and mature circRNA sequences
- Searches RBPs binding to a circRNA and to sequences upstream/downstream of the circRNA
- Identifies RBPs binding to the circRNA junctions
- Identifies miRNAs targeting a circRNA
- Designs divergent primers for circRNAs
- Designs siRNAs Specific to circRNA



Circ2Traits: a comprehensive database for circular RNA potentially associated with disease and traits

Suman Ghosal¹, Shaoli Das¹, Rituparno Sen², Piyali Basak³ and Jayprokas Chakrabarti^{1,2}*

<http://gyanxet-beta.com/circdb/>

收集与人类疾病或性状潜在关联的circRNA数据库。通过预测miRNAs和人类的蛋白质编码基因、长链非编码基因及**环状RNA**间的相互作用关系，构建了相互作用网络，并对miRNAs-circRNA相互作用组中的蛋白编码基因进行了GO富集分析；此外，将与疾病相关的SNPs位点定位到circRNA基因座上，并鉴定了**环状RNAs**上的Ago相互作用位点。

Cancer-Specific CircRNA Database

GRCh37 GRCh38 TUTORIAL CONTACT US DOWNLOAD CSCD

Cancer-specific All Samples All Genes All Cellular Location chr16:70301561|70311057

Search Result (GRCh37)

Gene	Type	CircRNA ID	UCSC	Sample Source	Location	Annotation	Ratio(circRNA/linear)	Spliced
AIBO	cancer	chr19:58864387 58864686	UCSC	HepG2_2	---	mRNA.lncRNA	0.000000000	---
AIBO	cancer	chr19:58862265 58862547	UCSC	HepG2_nuclear_2	---	mRNA.lncRNA	0.000000000	---
AIBO-AS1	cancer	chr19:58864387 58864686	UCSC	HepG2_2	---	mRNA.lncRNA	0.000000000	---
AIBO-AS1	cancer	chr19:58862265 58862547	UCSC	HepG2_nuclear_2	---	mRNA.lncRNA	0.000000000	---
AICF	cancer	chr10:52601621 52601729	UCSC	HepG2_2	exon	mRNA	0.4941071296	---
AICF	cancer	chr10:52580311 52580409	UCSC	HepG2_4.HepG2_insoluble_cytoplasmic_2	exon	mRNA	0.5129644451	---
AICF	cancer	chr10:52626949 52627310	UCSC	HepG2_nuclear_1	intron	mRNA	0.4926579451	---
AICF	cancer	chr10:52580311 52619145	UCSC	HepG2_cytosolic_3	exon	mRNA	0.7495774197	---
AICF	cancer	chr10:52591921 52592883	UCSC	HepG2_nuclear_2	intron	mRNA	0.4910057449	---
AICF	cancer	chr10:52593484 52594164	UCSC	HepG2_nuclear_2	intron	mRNA	0.4910057449	---
AICF	cancer	chr10:52610424 52619145	UCSC	HepG2_membrane_1	exon	mRNA	0.6292055846	---
AICF	cancer	chr10:52587890 52603882	UCSC	HepG2_cytosolic_4	exon	mRNA	0.7343636479	---
AICF	cancer	chr10:52582117 52588055	UCSC	HepG2_cytosolic_1	exon	mRNA	0.5573679239	---
AICF	cancer	chr10:52561026 52561202	UCSC	HepG2_nuclear_1	exon	mRNA	0.4926579451	---
AICF	cancer	chr10:52619801 52622770	UCSC	HepG2_3	exon	mRNA	0.5048564533	---
AICF	cancer	chr10:52596122 52596185	UCSC	HepG2_nuclear_1	intron	mRNA	0.4926579451	---
AICF	cancer	chr10:52601621 52623840	UCSC	HepG2_insoluble_cytoplasmic_2.HepG2_cytosolic_4	exon	mRNA	0.5960009411	---
AICF	cancer	chr10:52595833 52620069	UCSC	HepG2_cytosolic_3	exon	mRNA	0.7495774197	---

30 Page 1 of 9624 Displaying 1 to 30 of 288715 items

Overview Gene Transcript CircRNA Splice

AIRC

AIRC-EMT00000261772.12.1

MATS splicing events

Overview CircRNA MRE RBP ORF

ID	CircRNA ID	Family	species	MSA Start	MSA End	Site Type
1	chr16:70296269;70298971	miR-1199-5p/6751-3p	9606	90	95	6mer
2	chr16:70296269;70298971	miR-1252-5p	9606	50	56	7mer-1a
3	chr16:70296269;70298971	miR-1287-5p	9606	35	41	7mer-1a
4	chr16:70296269;70298971	miR-1288-5p	9606	76	81	6mer
5	chr16:70296269;70298971	miR-15a-3p	9606	80	85	6mer
6	chr16:70296269;70298971	miR-187-5p	9606	61	66	6mer
7	chr16:70296269;70298971	miR-211-3p	9606	85	91	7mer-m8
8	chr16:70296269;70298971	miR-3135b	9606	35	41	7mer-1a

武汉大学何春江教授和UT health Science Center韩冷教授

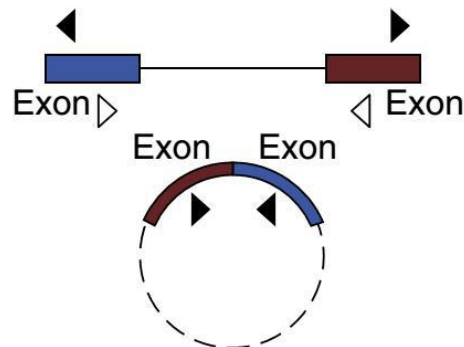
<http://gb.whu.edu.cn/CSCD>

19种肿瘤类型的87种细胞系及141种正常细胞的circRNA数据

- ✓ 1. 如何鉴定circRNA的存在
- ✓ 2. 如何设计qPCR引物
- ✓ 3. 如何设计siRNA;
- ✓ 4. 如何进行构建过表达载体

1. 如何鉴定circRNA的存在

1. 设计正向引物和跨拼接点的反向引物，扩增后进行测序或电泳，检测其存在；
2. 设计探针进行杂交后，Northern blot进行鉴定；
3. 设计跨拼接点的原位杂交探针，判断circRNA表达整体丰度和表达定位。



◄◄ Divergent primers
 ◄◄ Convergent primers

Convergent

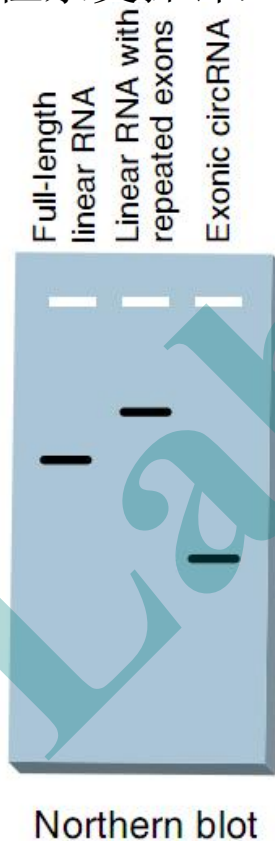


Divergent

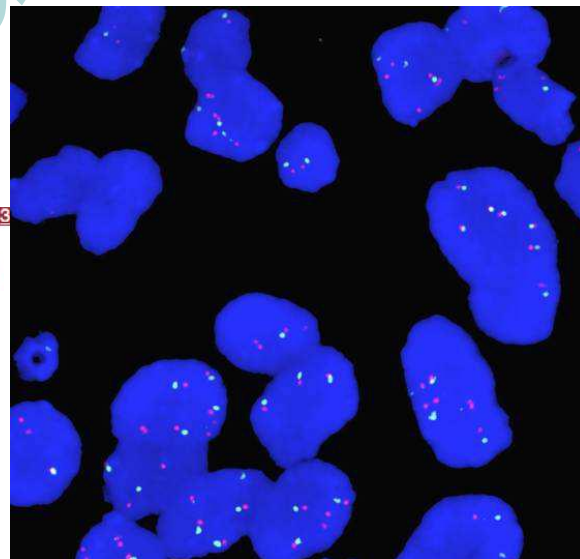


gDNA cDNA

gDNA cDNA

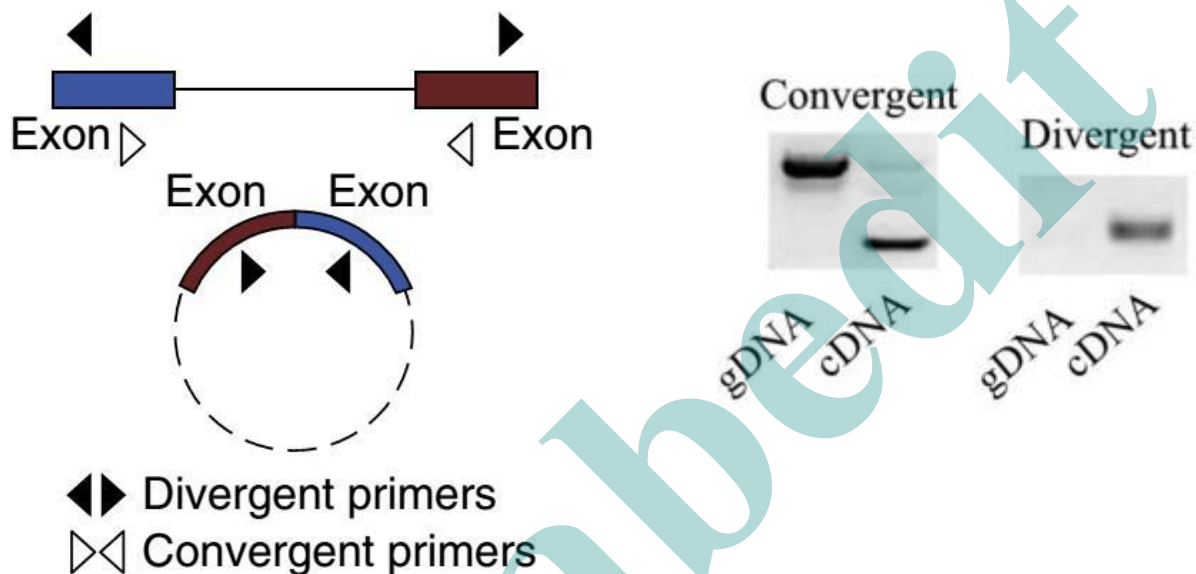


Exonic circRNA



Northern blot

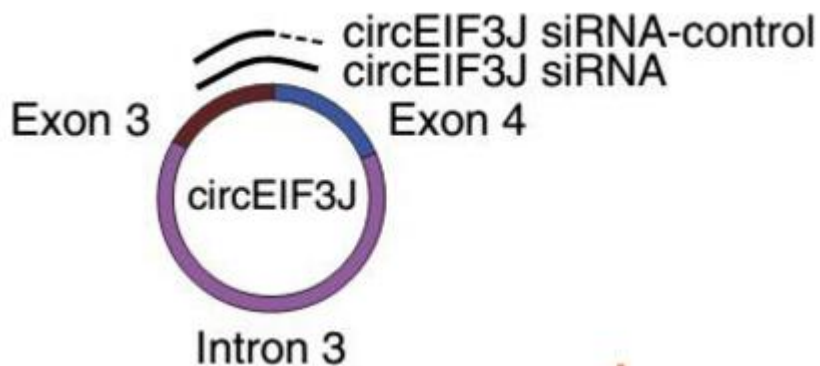
2. 如何设计qPCR引物



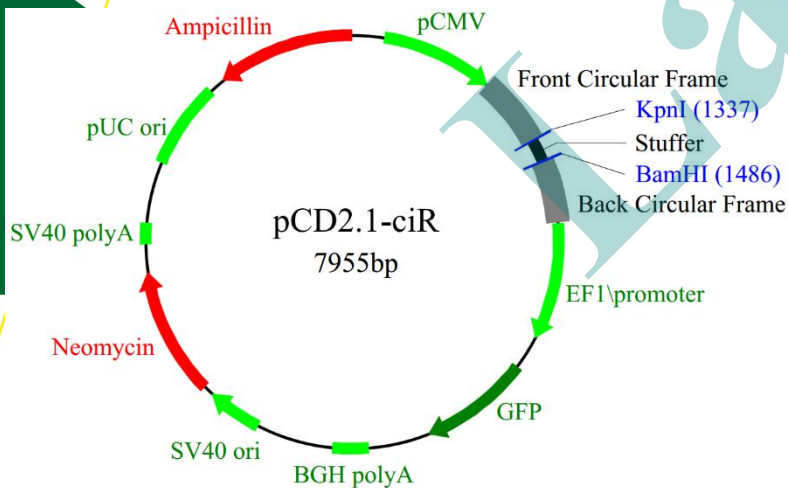
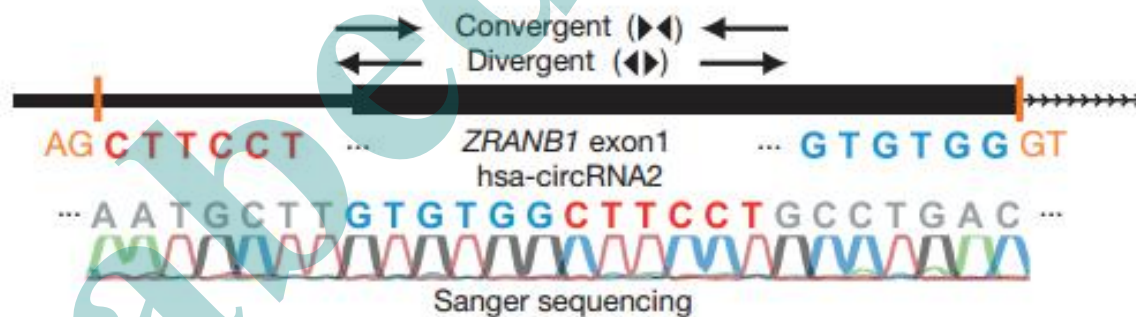
在明确拼接位点的前提下，设计的circRNA引物时，其扩增产物要包含该位点；并区别于线性mRNA的引物设计方法。扩增后进行进行比较和鉴定。

3. 如何设计siRNA；

4. 如何进行构建过表达载体



3.在设计siRNA时，要设计跨拼接位点的siRNA才能真正实现对circRNA的干扰；否则可能会靶向相应的mRNA；



4.目前提供的circRNA的过表达载体中，拼接装置已经是载体的一部分，只需要将circRNA的序列构入载体，即可实现circRNA的过表达。



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