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High Impact Factor References

吉玛基因

www.genepharma.com

目录

介绍

吉玛基因（NEEQ:430601）作为中国小核酸产业全链条技术服务商，自2003年由张佩琢博士带领海归团队创立以来，以RNAi技术为核心，构建了从 RNA 单体合成到新药研发的完整产业链。公司通过ISO9001与ISO13485质量体系认证，截止2025年底，累计SCI文献引用超80000篇，服务全球 7000多家合作伙伴，授权专利71项，是国内核酸科研服务与小核酸药物开发领域的领先品牌。

目前公司拥有处于国际先进水平的 siRNA 化学合成的全部核心技术，包括 RNA 单体合成技术、普通和修饰的 siRNA oligo 合成技术、核酸荧光标记技术、多种核苷酸化学修饰技术、shRNA 质粒载体构建技术，慢病毒载体构建以及包装技术、microRNA 荧光定量 PCR 检测试剂盒、荧光定量PCR 探针合成技术及其荧光定量 PCR、RNA Fish 检测技术等。在基因编辑技术上，公司拥有化学合成 gRNA、载体构建、病毒包装等多种平台，结合载体构建及直接使用 Cas-9 蛋白等方法实现基因编辑。在此基础上，吉玛公司已经发展形成强大的细胞技术平台，包括细胞增殖检测(MTT & CCK-8)、细胞凋亡检测（Annexin V/PI)、细胞迁移&侵袭实验(Transwell)、酶联免疫吸附实验（ELISA）等。此外，公司也建立了规范的 SPF 级动物房，开展转基因动物、PDX 模型建立和应用等技术服务。拥有一个近千平米的三类诊断试剂 GMP 生产车间和 1500 平方米的 RNA 药物中试车间。

公司产品涵盖化学合成的 RNA 单体，普通和修饰的 siRNA oligo，生物大分子标记用荧光染料；生物合成 siRNA、shRNA；转录编码 shRNA 的 DNAs、转录编码 shRNA 的质粒载体；慢病毒载体 lentiviurs 的构建以及包装，基于化学合成的 RNAi 的全程服务；基于载体调控的 shRNA RNAi全程服务；siRNA 相关试剂和 RNA 技术相关产品的销售；microRNA 荧光定量 PCR 检测试剂盒、荧光定量 PCR 探针和引物、荧光定量 PCR 检测服务；基因编辑相关试剂和技术服务；转基因动物；常用的分子生物学试剂、实验耗材销售等。

qPCR 检测试剂盒

Open
ORIGINAL ARTICLE

Cell Research (2015) 25:588-603.
© 2015 IBCB, SIBS, CAS All rights reserved 1001-0602/15
www.nature.com/cr

Epigenetic silencing of microRNA-149 in cancer-associated fibroblasts mediates prostaglandin E2/interleukin-6 signaling in the tumor microenvironment

Pu Li[1,*], Jing-Xuan Shan[3,*], Xue-Hua Chen[1,*], Di Zhang[2,*], Li-Ping Su[1], Xiu-Ying Huang[2], Bei-Qin Yu[1], Qiao-Ming Zhi[1], Cheng-Long Li[1], Ya-Qing Wang[2], Sara Tomei[3], Qu Cai[1], Jun Ji[1], Jian-Fang Li[1], Lotfi Chouchane[3], Ying-Yan Yu[1], Fang-Zhen Sun[2], Zhi-Heng Xu[2], Bing-Ya Liu[1], Zheng-Gang Zhu[1]

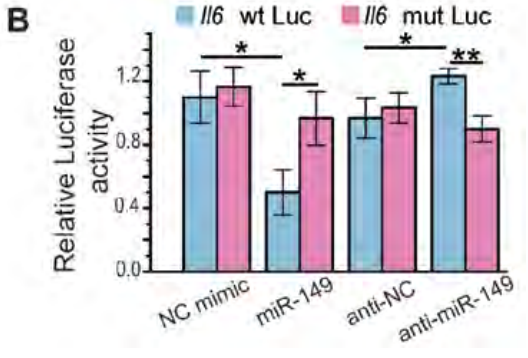
Tumor initiation and growth depend on its microenvironment in which cancer-associated fibroblasts (CAFs) in tumor stroma play an important role. Prostaglandin E2 (PGE2) and interleukin (IL)-6 signal pathways are involved in the crosstalk between tumor and stromal cells. However, how PGE2-mediated signaling modulates this crosstalk remains unclear. Here, we show that microRNA (miR)-149 links PGE2 and IL-6 signaling in mediating the crosstalk between tumor cells and CAFs in gastric cancer (GC). miR-149 inhibited fibroblast activation by targeting IL-6 and miR-149 expression was substantially suppressed in the CAFs of GC. miR-149 negatively regulated CAFs and their effect on GC development both in vitro and in vivo. CAFs enhanced epithelial-to-mesenchymal transition (EMT) and the stem-like properties of GC cells in a miR-149-IL-6-dependent manner. In addition to IL-6, PGE2 receptor 2 (PTGER2/EP2) was revealed as another potential target of miR-149 in fibroblasts. Furthermore, H. pylori infection, a leading cause of human GC, was able to induce cyclooxygenase-2 (COX-2)/PGE2 signaling and to enhance PGE2 production, resulting in the hypermethylation of miR-149 in CAFs and increased IL-6 secretion. Our findings indicate that miR-149 mediates the crosstalk between tumor cells and CAFs in GC and highlight the potential of interfering miRNAs in stromal cells to improve cancer therapy.

Keywords: microRNA-149; epigenetic silencing; cancer-associated fibroblasts; PGE2; IL-6

Cell Research
2015; 25(5): 588-603
Impact Factor: 44.1

Materials and Methods

The expression levels of miRNAs were measured by **miRNAs qPCR Kit** (**GenePharma**, Shanghai, China) according to the manufacturer's instructions.



Xiong et al. Journal of Hematology & Oncology (2019) 12:97
https://doi.org/10.1186/s13045-019-0777-7

Journal of Hematology & Oncology

RESEARCH Open Access

Long noncoding RNA GSTM3TV2 upregulates LAT2 and OLR1 by competitively sponging let-7 to promote gemcitabine resistance in pancreatic cancer

Guangbing Xiong[1,2†], Chang Liu[3†], Gang Yang[1†], Mengyu Feng[1], Jianwei Xu[1,4], Fangyu Zhao[1], Lei You[1], Li Zhou[1], Lianfang Zheng[5], Ya Hu[1], Xiaowo Wang[3*], Taiping Zhang[1,6*] and Yupei Zhao[1*]

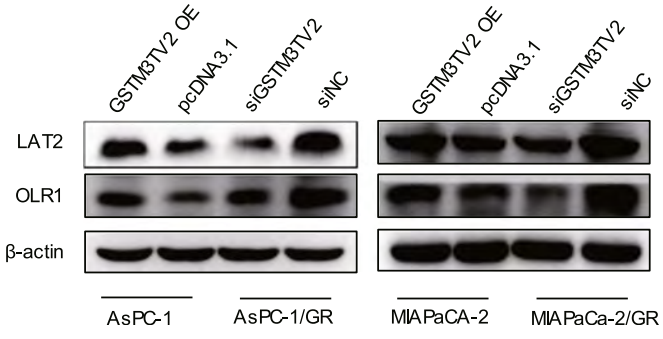
Abstract

Background: Chemoresistance is one of the main causes of poor prognosis in pancreatic cancer patients. Understanding the mechanisms implicated in chemoresistance of pancreatic cancer is critical to improving patient outcomes. Recent evidences indicate that the long noncoding RNAs (lncRNAs) are involving in chemoresistance of pancreatic cancer. However, the mechanisms of lncRNAs contribute to resistance in pancreatic cancer and remain largely unknown. The objective of this study is to construct a chemoresistance-related lncRNA-associated competing endogenous RNA (ceRNA) network of pancreatic cancer and identify the key lncRNAs in regulating chemoresistance of the network.
Methods: Firstly, lncRNA expression profiling of gemcitabine-resistant pancreatic cancer cells was performed to identify lncRNAs related to chemoresistance by microarray analysis. Secondly, with insights into the mechanism of ceRNA, we used a bioinformatics approach to construct a chemoresistance-related lncRNAs-associated ceRNA network. We then identified the topological key lncRNAs in the ceRNA network and demonstrated its function or mechanism in chemoresistance of pancreatic cancer using molecular biological methods. Further studies evaluated its expression to assess its potential association with survival in patients with pancreatic cancer.

Journal of Hematology & Oncology
2019 Sep 12; 12:97
Impact Factor: 28.5

Materials and Methods

To synthesize cDNA, total RNA was reverse transcribed using a PrimeScript RT Reagent Kit (Takara, Japan) and a **miRNA qPCR Quantitation Kit** (**GenePharma**, Shang-hai, China) according to the manufacturer's instructions.



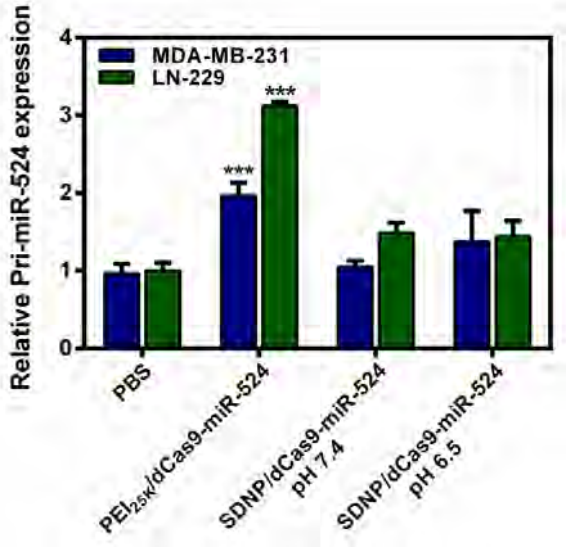
FULL PAPER
Tumor Suppression
ADVANCED SCIENCE
www.advancedscience.com

Multistage Delivery Nanoparticle Facilitates Efficient CRISPR/dCas9 Activation and Tumor Growth Suppression In Vivo

Qi Liu, Kai Zhao, Chun Wang, Zhanzhan Zhang, Chunxiong Zheng, Yu Zhao, Yadan Zheng, Chaoyong Liu, Yingli An, Linqi Shi, Chunsheng Kang,* and Yang Liu**

CRISPR/dCas9 systems can precisely control endogenous gene expression without interrupting host genomic sequence and have provided a novel and feasible strategy for the treatment of cancers at the transcriptional level. However, development of CRISPR/dCas9-based anti-cancer therapeutics remains challenging due to the conflicting requirements for the design of the delivery system: a cationic and membrane-binding surface facilitates the tumor accumulation and cellular uptake of the CRISPR/dCas9 system, but hinders the circulating stability in vivo. Here, a multistage delivery nanoparticle (MDNP) that can achieve tumor-targeted delivery of CRISPR/dCas9 systems and restore endogenous microRNA (miRNA) expression in vivo is described. MDNP is designed as a core-shell structure in which the shell is made of a responsive polymer that endows MDNP with the capability to present different surface properties in response to its surrounding microenvironment, allowing the MNDP overcoming multiple physiological barriers and delivering the payload to tumor tissues with an optimal efficiency. Systemic administration of MDNP/dCas9-miR-524 to tumor-bearing mice achieved effective upregulation of miR-524 in tumors, leading to the simultaneous interferences of multiple signal pathways related to cancer cell proliferation and presenting remarkable tumor growth retardation, suggesting the feasibility of utilizing MDNP to achieve tumor-targeting delivery of CRISPR/dCas9 with sufficient levels to realize its therapeutic effects.

Advanced Science
2019; 6: 1801423
Impact Factor: 15.1



Materials and Methods

Hairpin-it miRNA qPCR Quantitation Kit was obtained from **GenePharma** Biotech (Shanghai, China).

ADVANCED SCIENCE Open Access
www.advancedscience.com

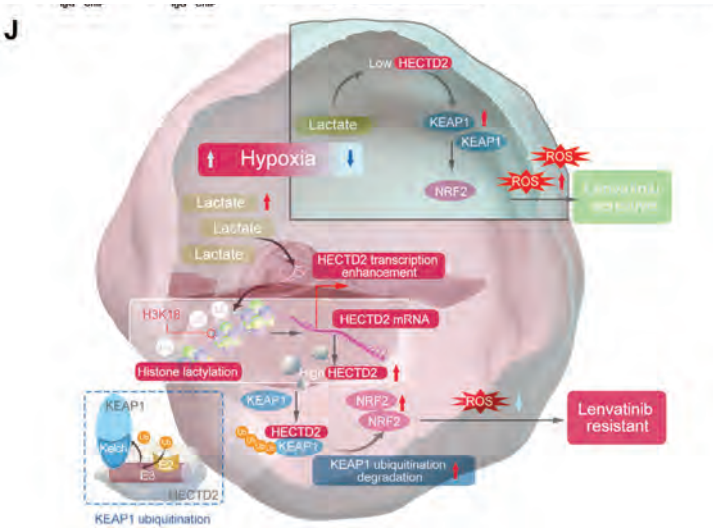
Lactylation-Driven HECTD2 Limits the Response of Hepatocellular Carcinoma to Lenvatinib

Runyu Dong, Yao Fei, Yiren He, Peng Gao, Bo Zhang, Menglin Zhu, Zhixiong Wang, Longfei Wu, Shuai Wu, Xiaoming Wang, Juan Cai, Zhiqiang Chen,* and Xueliang Zuo**

Drug resistance remains a major hurdle for the therapeutic efficacy of lenvatinib in hepatocellular carcinoma (HCC). However, the underlying mechanisms remain largely undetermined. Unbiased proteomic screening is performed to identify the potential regulators of lenvatinib resistance in HCC. Patient-derived organoids, patient-derived xenograft mouse models, and DEN/CCl_4 induced HCC models are constructed to evaluate the effects of HECTD2 both in vitro and in vivo. HECTD2 is found to be highly expressed in lenvatinib-resistant HCC cell lines, patient tissues, and patient-derived organoids and xenografts. In vitro and in vivo experiments demonstrated that overexpression of HECTD2 limits the response of HCC to lenvatinib treatment. Mechanistically, HECTD2 functions as an E3 ubiquitin ligase of KEAP1, which contributes to the degradation of KEAP1 protein. Subsequently, the KEAP1/NRF2 signaling pathway initiates the antioxidative response of HCC cells. Lactylation of histone 3 on lysine residue 18 facilitates the transcription of HECTD2. Notably, a PLGA-PEG nanoparticle-based drug delivery system is synthesized, effectively targeting HECTD2 in vivo. The NPs achieved tumor-targeting, controlled-release, and biocompatibility, making them a promising therapeutic strategy for mitigating lenvatinib resistance. This study identifies HECTD2 as a nanotherapeutic target for overcoming lenvatinib resistance, providing a theoretical basis and translational application for HCC treatment.

1. Introduction

Primary liver cancer ranks as the sixth most frequently diagnosed cancer and the third leading cause of cancer-related death worldwide.[1] Hepatocellular carcinoma (HCC) accounts for over 80% of primary liver cancer cases.[2] Surgical resection and liver transplantation remain the only curative treatments for patients with HCC. However, most HCC cases are diagnosed at an advanced stage, rendering them ineligible for surgery. Lenvatinib, a multi-targeted tyrosine kinase inhibitor that effectively targets VEGFR1 to VEGFR3, FGFR1 to FGFR4, PDGFRα, KIT, and RET, has been approved as a first-line therapeutic agent for advanced HCC since 2018.[3] However, drug resistance remains a major obstacle to its therapeutic efficacy. Many patients develop either acquired or intrinsic lenvatinib resistance, significantly limiting its clinical application and effectiveness.[4] Therefore, understanding the molecular mechanisms underlying lenvatinib resistance is crucial for developing effective therapeutic strategies and improving patients with HCC prognosis.



Advanced Science
2025 The Author(s)
Impact Factor: 14.3

Materials and Methods

qRT-PCR primers were designed and synthesized by **GenePharma** (Shanghai, China).

Journal of Advanced Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of Advanced Research

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

Gymconopin C exhibits anti-non-small cell lung cancer effect by regulating miR-6777-5p/ADRB2 pathway to promote mitophagy

Xue Li [a,b], Mingyu Han [a], Limei Zhang [a], Xiaofang Xie [b], Chenying Li [c], Heng Zhang [a], Junsha An [a], Jianning Yang [a], Shuang Pu [a], Yue Duan [a], Changnian Yang [d,e,*], Cheng Peng [b,*], Hailin Tang [f], Fu Peng [a,*]

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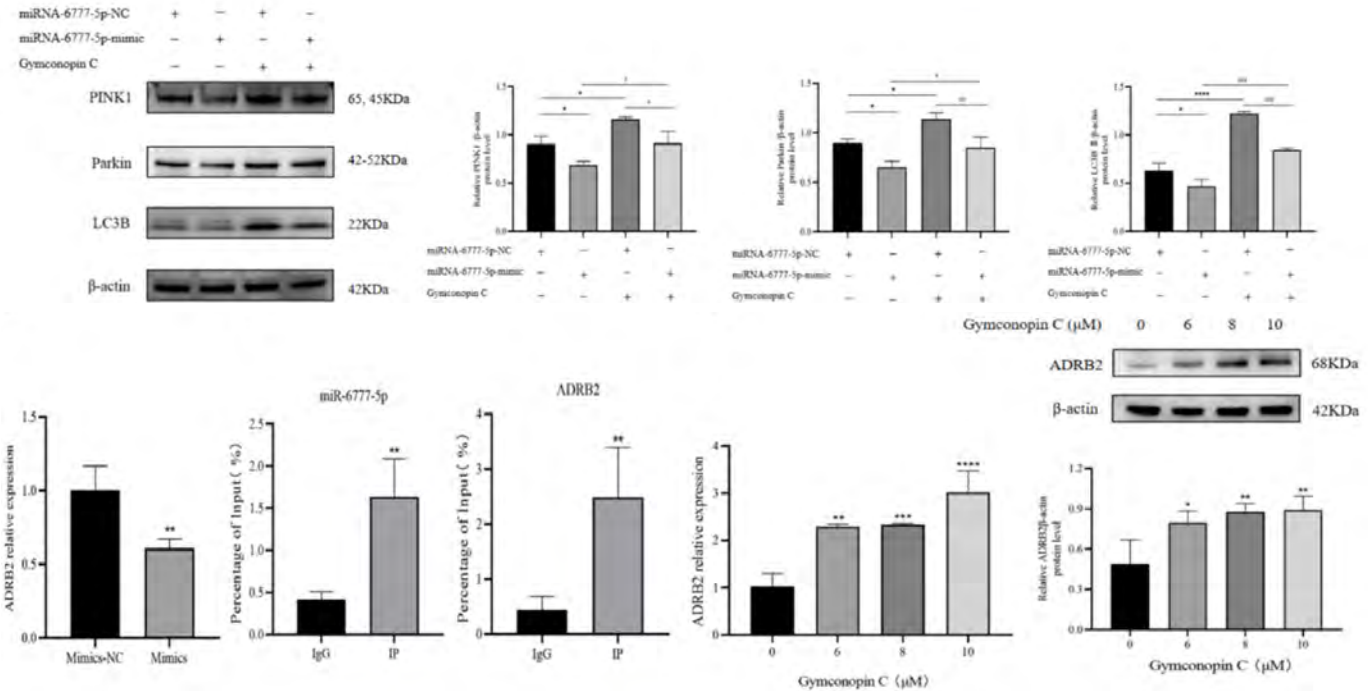
[b] Key Laboratory of Standardization of Chinese Medicine (Chengdu University of Traditional Chinese Medicine), Ministry of Education, Chengdu 611137, China
[c] School of Obstetrics and Pediatrics, Guangdong Medical University, Zhanjiang, China
[d] The First Clinical College, Guangdong Medical University, Zhanjiang, China
[e] Medical Research Institute, Guangdong Provincial People's Hospital, Guangzhou, China
[f] State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou 510060, China



Journal of Advanced Research

(2025) 23:471

Impact Factor: 13

Materials and Methods

was performed using **Hairpin-it miRNAs RT-qPCR Quantification kit** (1406, **Genepharma**, China)

Journal of Nanobiotechnology

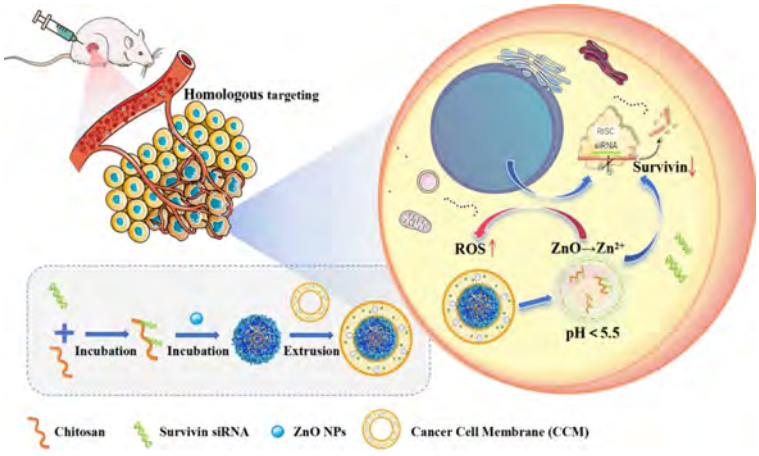
RESEARCH Open Access

Cancer cell membrane-camouflaged pH-responsive nanoparticles for enhancing siRNA effect and synergistic anti-tumor therapy

Jie Zhang[1,2,3†], Yun Peng Zhang[1,2,3†], Qi Sun[1,2,3], Yaoqi Wang[1,2,3], Dong Mei[3,4], Xiaoling Wang[3,4], Yan Su[3,5], Yang Tian[1,2,3], Ran Huo[1,2,3], Danni Liu[1,2,3], Siyu Liu[1,2,3], Myagmarsuren Baldan[1,2,3], Shuang Zhang[1,2,3*] and Chunying Cui[1,2,3*]

Abstract

RNA-based therapies, especially small interfering RNA (siRNA), have attracted extensive attention for tumor treatment. However, most siRNA can't exert a therapeutic effect due to a lack of targeting to tumor cells and entrapment in lysosomes upon administration. To address the challenges associated with siRNA delivery, a delivery system was developed using zinc oxide nanoparticles (ZnO NPs) coated with cancer cell membranes. ZnO nanoparticles (ZnO NPs) have been recognized as effective pH-responsive nanoparticles and are widely used in the development of pH-responsive drug delivery systems. The ZnO NPs were combined with chitosan to encapsulate siRNA, allowing for dissolution in acidic lysosomes and the subsequent release of siRNA and chitosan complexes. The dissolution of ZnO NPs would also disrupt lysosomes, facilitating the escape of siRNA and enhancing its gene silencing effect. However, the chitosan and ZnO NPs nano-complexes (CS/ZnO@siRNA) were unstable in solution and lacked a specific targeting effect for tumor cells. Thus, a homologous cancer cell membrane was coated onto the nanoparticles, which has been shown to be an effective strategy for enhancing their stability and targeting capabilities. Moreover, ZnO NPs not only dissolve in acidic lysosomes to enhance the efficacy of siRNA but also elevate oxidative stress levels in cells, leading to the induction of cellular apoptosis. It was demonstrated both *in vitro* and in vivo that the ZnO NPs could synergistically combine with the anti-tumor siRNA (siSurvivin) to inhibit the growth of the 4T1 tumor. Altogether, the developed drug delivery system (CCM-CS/ZnO@siSurvivin) offers a new strategy for enhancing the therapeutic effect of siRNA, while synergistically inhibiting tumor growth.



JOURNAL OF NANOBIOTECHNOLOGY

(2025) 23:471

Impact Factor: 12.6

Materials and Methods

probe Survivin customized gene **qRT-PCR quantitative kit, GAPDH/β-actin calibration qRT-PCR quantitative kit** were pur-chased from **GenePharma**

Li *et al. J Exp Clin Cancer Res* (2022) 41:297
https://doi.org/10.1186/s13046-022-02513-z

Journal of Experimental & Clinical Cancer Research

RESEARCH Open Access

STAT3/miR-130b-3p/MBNL1 feedback loop regulated by mTORC1 signaling promotes angiogenesis and tumor growth

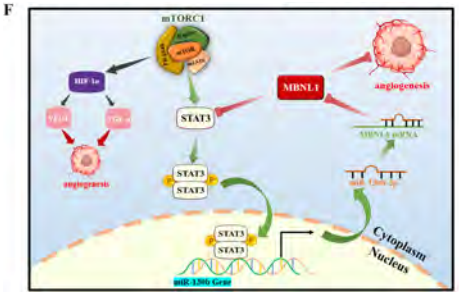
Hongwu Li[1,2,3†], Ping Liu[1,2,3†], Dapeng Li[1†], Zixi Wang[3†], Zhao Ding[1], Meng Zhou[4], Xu Chen[3], Manli Miao[3], Junli Ding[5], Wei Lin[6*], Yehai Liu[1*] and Xiaojun Zha[3*]

Abstract

Background: Aberrantly activated mammalian target of rapamycin complex 1 (mTORC1) plays a vital role in tumor angiogenesis, but its precise mechanisms are still unclear.

Methods: Micro-RNA-130b-3p (miR-130b-3p) expression in mTORC1-activated and control cells was examined by quantitative real-time PCR (qRT-PCR). MiR-130b-3p levels and their correlation with mTORC1 activity were evaluated by analyzing publicly available databases and in-house head and neck squamous cell carcinoma (HNSCC) tissues. The role of miR-130b-3p in mTORC1-mediated angiogenesis and tumor growth was examined using tube formation assay, chicken chorioallantoic membrane assay, cell line − derived xenograft models, and an HNSCC patient-derived xenograft (PDX) model. The regulatory mechanisms among signal transducer and activator of transcription 3 (STAT3), miR-130b-3p, and muscleblind-like protein 1 (MBNL1) were investigated via bioinformatics analyses, qRT-PCR, western blot, RNA immunoprecipitation, immunofluorescence, luciferase reporter assay, and chromatin immunoprecipitation assay.

Results: Elevated miR-130b-3p enhanced the angiogenic and tumorigenic abilities of mTORC1-activated cells both in vitro and in vivo. STAT3, a downstream effector of mTORC1, transactivated miR-130b-3p by direct binding promoter of the miR-130b gene. MBNL1 was identified as a direct target of miR-130b-3p. MBNL1 depletion rescued the com-promised angiogenesis and tumor growth caused by miR-130b-3p inhibition. MiR-130b-3p levels were significantly upregulated and positively correlated with mTORC1 signaling in multiple cancers. MiR-130b-3p inhibition attenuated tumor angiogenesis and growth in an HNSCC PDX model. MBNL1 feedback inhibited STAT3 activation in mTORC1-activated cells.



JOURNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH
2022 Dec;41(1):1-21
Impact Factor: 11.3

Materials and Methods

expression of miR-130b-3p was detected using the **Hairpin-itTM micro-RNAs qPCR Quantitation Kit** (**GenePharma**, Shanghai, China) according to the producer's instructions.
Transient transfection of mouse miR-130b-3p mimics, inhibitors, and the **negative control** (**GenePharma**) was conducted with Lipofectamine RNAiMax.
A fragment of 330-bp MBNL1 3′-untranslated region (3′-UTR) containing the putative binding site for miR-130b-3p was gener-ated by PCR and cloned into the **p-miRGLO firefly luciferase vector** (**GenePharma**).
The P3 xenografts were treated intratumorally with either antagomiR-130b-3p (a 2′-OMe + 5′-chol–modified miR-130b-3p inhibitor) or the **scramble control antagomiR-NC** (**GenePharma**).

Journal of Controlled Release 370 (2024) 405–420

Contents lists available at ScienceDirect

Journal of Controlled Release

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

Small extracellular vesicles of organoid-derived human retinal stem cells remodel Müller cell fate via miRNA: A novel remedy for retinal degeneration

Shudong Huang [a,b], Yuxiao Zeng [a,b], Qiang Guo [a,b], Ting Zou [a,b,c,*], Zheng Qin Yin [a,b,*]

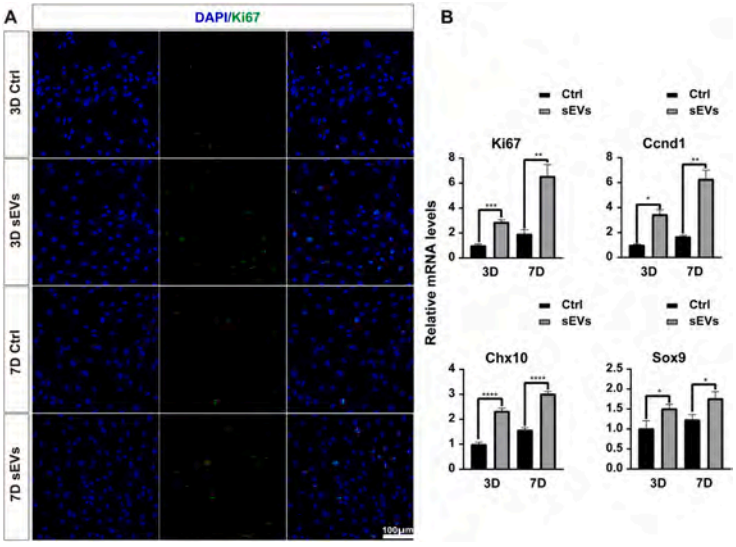
[a] Southwest Hospital/Southwest Eye Hospital, Third Military Medical University (Army Medical University), Chongqing 400038, China
[b] Key Lab of Visual Damage and Regeneration & Restoration of Chongqing, Chongqing 400038, China
[c] Department of Ophthalmology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China

ARTICLE INFO

Keywords:
Small extracellular vesicle
Stem cells
Retinal organoids
Retinal degenerative diseases
Müller cells

ABSTRACT

Remodeling retinal Müller glial fate, including gliosis inhibition and pro-reprogramming, represents a crucial avenue for treating degenerative retinal diseases. Stem cell transplantation exerts effects on modulating retinal Müller glial fate. However, the optimized stem cell products and the underlying therapeutic mechanisms need to be investigated. In the present study, we found that retinal progenitor cells from human embryonic stem cell-derived retinal organoids (hERO-RPCs) transferred extracellular vesicles (EVs) into Müller cells following subretinal transplantation into RCS rats. Small EVs from hERO-RPCs (hERO-RPC-sEVs) were collected and were found to delay photoreceptor degeneration and protect retinal function in RCS rats. hERO-RPC-sEVs were taken up by Müller cells both in vivo and in vitro, and inhibited gliosis while promoting early dedifferentiation of Müller cells. We further explored the miRNA profiles of hERO-RPC-sEVs, which suggested a functional signature associated with neuroprotection and development, as well as the regulation of stem cell and glial fate. Mechanistically, hERO-RPC-sEVs might regulate the fate of Müller cells by miRNA-mediated nuclear factor I transcription factors B (NFIB) downregulation. Collectively, our findings offer novel mechanistic insights into stem cell therapy and promote the development of EV-centered therapeutic strategies.



JOURNAL OF CONTROLLED RELEASE
Available online 5 May 2024
Impact Factor: 10.8

Materials and Methods
For miRNAs, the process involved the conversion of the total RNA into cDNA which was then used for quantitative PCR using the **Hairpin microRNA** and **RT-PCR quantitation kit** (#E22001, **Gene-Pharma,** China). The expression level of each mRNA or miRNA was compared to th

Journal of Nanobiotechnology

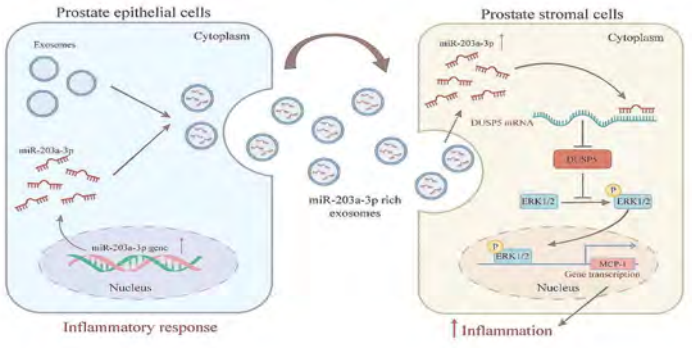
RESEARCH Open Access

Epithelial cells derived exosomal miR-203a-3p facilitates stromal inflammation of type IIIA chronic prostatitis/chronic pelvic pain syndrome by targeting DUSP5 and increasing MCP-1 generation

Guojing Song[1†], Fuhan Zhao[1†], Rongrong Ni[2], Bingqian Deng[2], Saipeng Chen[1], Ruimin Hu[1], Jun Zheng[1], Yiji Peng[1], Heting Liu[2], Yang Luo[3], Zhansong Zhou[1*], Gang Huang[2*] and Wenhao Shen[1*]

Abstract
Increased proinflammatory cytokines and infiltration of inflammatory cells in the stroma are important pathological features of type IIIA chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS-A), and the interaction between stromal cells and other cells in the inflammatory microenvironment is closely related to the inflammatory process of CP/CPPS-A. However, the interaction between stromal and epithelial cells remains unclear. In this study, inflammatory prostate epithelial cells (PECs) released miR-203a-3p-rich exosomes and facilitated prostate stromal cells (PSCs) inflammation by upregulating MCP-1 expression. Mechanistically, DUSP5 was identified as a novel target gene of miR-203a-3p and regulated PSCs inflammation through the ERK1/2/MCP-1 signaling pathway. Meanwhile, the effect of exosomes derived from prostatic fluids of CP/CPPS-A patients was consistent with that of exosomes derived from inflammatory PECs. Importantly, we demonstrated that miR-203a-3p antagomirs-loaded exosomes derived from PECs targeted the prostate and alleviated prostatitis by inhibiting the DUSP5-ERK1/2 pathway. Collectively, our findings provide new insights into underlying the interaction between PECs and PSCs in CP/CPPS-A, providing a promising therapeutic strategy for CP/CPPS-A.

Keywords CP/CPPS-A, Exosomes, miR-203a-3p, DUSP5, Inflammation



Clinical and Translational Medicine
Song et al. Journal of Nanobiotechnology (2024) 22:236
Impact Factor: 10.8

Materials and Methods

Reverse transcription of miR-NAs or mRNAs was carried out using **the Hairpin-it™ miRNAs RT-PCR Quantitation Kit** (**Genepharma**, China)

NANO LETTERS
Letter
Cite This: Nano Lett. XXXX, XXX, XXX−XXX
pubs.acs.org/NanoLett

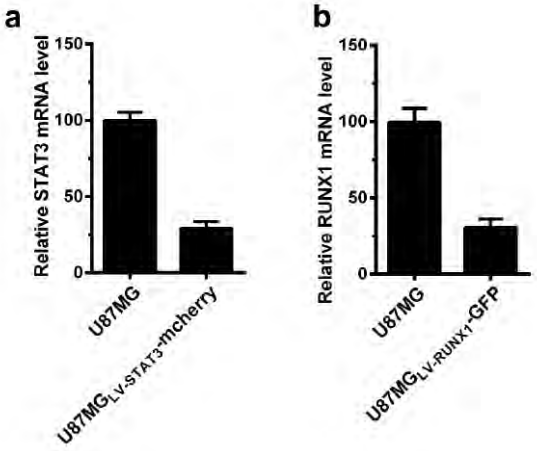
NanoRNP Overcomes Tumor Heterogeneity in Cancer Treatment

Qi Liu,[†] Jinquan Cai,[§] Yadan Zheng,[†] Yanli Tan,[∥] Yunfei Wang,[‡] Zhanzhan Zhang,[†] Chunxiong Zheng,[†] Yu Zhao,[†] Chaoyong Liu,[‡] Yingli An,[†] Chuanlu Jiang,*[,§] Linqi Shi,*[,†] Chunsheng Kang,*[,‡] and Yang Liu*[,†]

ABSTRACT: Tumor heterogeneity has been one of the most important factors leading to the failure of conventional cancer therapies due to the accumulation of genetically distinct tumor-cell subpopulations during the tumor development process. Due to the diversity of genetic mutations during tumor growth, combining the use of multiple drugs has only achieved limited success in combating heterogeneous tumors. Herein, we report a novel antitumor strategy that effectively addresses tumor heterogeneity by using a CRISPR/Cas9-based nanoRNP carrying a combination of sgRNAs. Such nanoRNP is synthesized from Cas9 ribonucleoprotein, any combinations of required sgRNAs, and a rationally designed responsive polymer that endows nanoRNP with high circulating stability, enhanced tumor accumulation, and the efficient gene editing in targeted tumor cells eventually. By carrying a combination of sgRNAs that targets STAT3 and RUNX1, the nanoRNP exhibited efficient gene expression disruptions on a heterogeneous tumor model with two subsets of cells whose proliferations were sensitive to the reduced expression of STAT3 and RUNX1, respectively, leading to the effective growth inhibition of the heterogeneous tumor. Considering the close relationship between tumor heterogeneity and cancer progression, resistance to therapy, and recurrences, nanoRNP provides a feasible strategy to overcome tumor heterogeneity in the development of more advanced cancer therapy against malignant tumors.

NANO LETTERS
2019 Oct 8; 19(11): 7662-72
Impact Factor: 10.8

Materials and Methods
Hairpin-it miRNA qPCR Quantitation Kit was obtained from **GenePharma** Biotech (Shanghai, China).



Journal of Nanobiotechnology

RESEARCH Open Access

Treg cells-derived exosomes promote blood-spinal cord barrier repair and motor function recovery after spinal cord injury by delivering miR-2861

Guang Kong[1,3†], Wu Xiong[2,3†], Cong Li[2,3†], Chenyu Xiao[3,4†], Siming Wang[2,3], Wenbo Li[2,3], Xiangjun Chen[3,4], Juan Wang[3,4], Sheng Chen[1], Yongjie Zhang[3,4*], Jun Gu[1*], Jin Fan[2,3*] and Zhengshuai Jin[1,2,3*]

Abstract

The blood-spinal cord barrier (BSCB) is a physical barrier between the blood and the spinal cord parenchyma. Current evidence suggests that the disruption of BSCB integrity after spinal cord injury can lead to secondary injuries such as spinal cord edema and excessive inflammatory response. Regulatory T (Treg) cells are effective anti-inflammatory cells that can inhibit neuroinflammation after spinal cord injury, and their infiltration after spinal cord injury exhibits the same temporal and spatial characteristics as the automatic repair of BSCB. However, few studies have assessed the relationship between Treg cells and spinal cord injury, emphasizing BSCB integrity. This study explored whether Treg affects the recovery of BSCB after SCI and the underlying mechanism. We confirmed that spinal cord angiogenesis and Treg cell infiltration occurred simultaneously after SCI. Furthermore, we observed significant effects on BSCB repair and motor function in mice by Treg cell knockout and overexpression. Subsequently, we demonstrated the presence and function of exosomes in vitro. In addition, we found that Treg cell-derived exosomes encapsulated miR-2861, and miR-2861 regulated the expression of vascular tight junction (TJs) proteins. The luciferase reporter assay confirmed the negative regulation of IRAK1 by miR-2861, and a series of rescue experiments validated the biological function of IRAKI in regulating BSCB. In summary, we demonstrated that Treg cell-derived exosomes could package and deliver miR-2861 and regulate the expression of IRAK1 to affect BSCB integrity and motor function after SCI in mice, which provides novel insights for functional repair and limiting inflammation after SCI.

Keywords Spinal cord injury, Regulatory T cells, Blood-spinal cord barrier, Exosomes, miRNA

JOURNAL OF NANOBIOTECHNOLOGY
2023 Oct 4;21(1):364
Impact Factor: 10.2

Materials and Methods

Total RNA from cells and exosomes was extracted using TRIzol reagent (Invitrogen, Carlsbad, CA, USA), the hairpin **itTM miRNA qPCR quantification kit** (**GenePharma**, China), and PrimeScript RT kit (Takara, Japan) to synthesize cDNA for miRNA and mRNA.

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Liu S, Chen J, Shi J, Zhou W, Wang L, Fang W, Zhong Y, Chen X, Chen Y, Sabri A, Liu S. M1-like macrophage-derived exosomes suppress angiogenesis and exacerbate cardiac dysfunction in a myocardial infarction microenvironment. Basic Res Cardiol. 2020 Feb 28;115(2):22. **IF: 9.5**

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Xiao F, Bai Y, Chen Z, et al. Downregulation of HOXA1 gene affects small cell lung cancer cell survival and chemoresistance under the regulation of miR-100. European Journal of Cancer. 2014 Feb 19. **IF: 8.4**

RNA FISH / Pulldown 探针和试剂盒

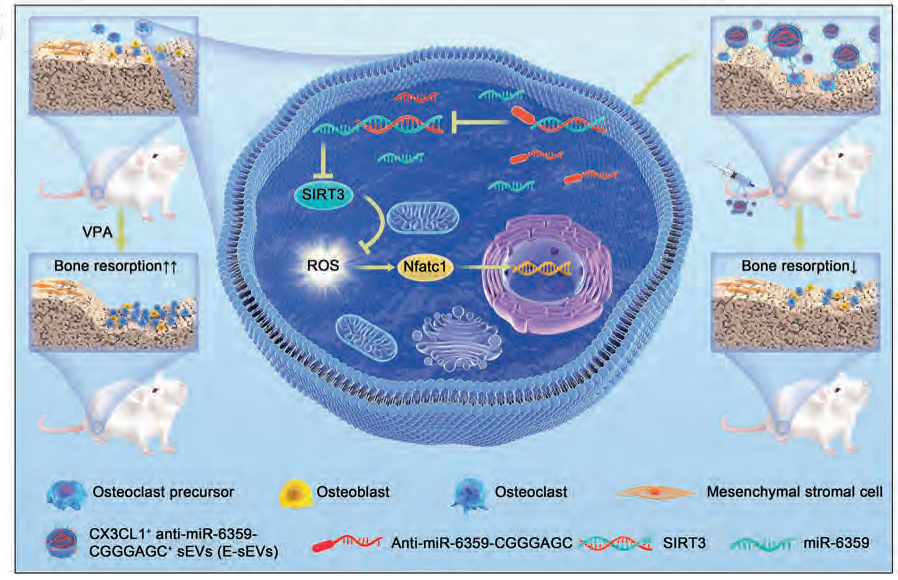
ARTICLE OPEN Signal Transduction and Targeted Therapy

Bone-targeting engineered small extracellular vesicles carrying anti-miR-6359-CGGGAGC prevent valproic acid-induced bone loss

Xudong Xie[1,2], Peng Cheng[1,2], Liangcong Hu[1,2], Wu Zhou[1,2], Detai Zhang[3], Samuel Knoedler[4,5], Guodong Liu[6], Yuan Xiong[1,2], Hang Xue[1,2], Yiqiang Hu[1,2], Barbara Kern[7,8], Doha Obed[4,9], Adriana C. Panayi[4,10], Lang Chen[1,2], Chenchen Yan[1,2], Ze Lin[1,2], Guandong Dai[11], Bobin Mi[1,2]✉, Yingze Zhang[1,12]✉ and Guohui Liu[1,2]✉

The clinical role and underlying mechanisms of valproic acid (VPA) on bone homeostasis remain controversial. Herein, we confirmed that VPA treatment was associated with decreased bone mass and bone mineral density (BMD) in both patients and mice. This effect was attributed to VPA-induced elevation in osteoclast formation and activity. Through RNA-sequencing, we observed a significant rise in precursor miR-6359 expression in VPA-treated osteoclast precursors in vitro, and further, a marked upregulation of mature miR-6359 (miR-6359) in vivo was demonstrated using quantitative real-time PCR (qRT-PCR) and miR-6359 fluorescent in situ hybridization (miR-6359-FISH). Specifically, the miR-6359 was predominantly increased in osteoclast precursors and macrophages but not in neutrophils, T lymphocytes, monocytes and bone marrow-derived mesenchymal stem cells (BMSCs) following VPA stimulation, which influenced osteoclast differentiation and bone-resorptive activity. Additionally, VPA-induced miR-6359 enrichment in osteoclast precursors enhanced reactive oxygen species (ROS) production by silencing the SIRT3 protein expression, followed by activation of the MAPK signaling pathway, which enhanced osteoclast formation and activity, thereby accelerating bone loss. Currently, there are no medications that can effectively treat VPA-induced bone loss. Therefore, we constructed engineered small extracellular vesicles (E-sEVs) targeting osteoclast precursors in bone and naturally carrying anti-miR-6359 by introducing of EXOmotif (CGGGAGC) in the 3′-end of the anti-miR-6359 sequence. We confirmed that the E-sEVs exhibited decent bone/osteoclast precursor targeting and exerted protective therapeutic effects on VPA-induced bone loss, but not on ovariectomy (OVX) and glucocorticoid-induced osteoporotic models, deepening our understanding of the underlying mechanism and treatment strategies for VPA-induced bone loss.

Signal Transduction and Targeted Therapy (2024)9:24 ; https://doi.org/10.1038/s41392-023-01726-8



Signal Transduction and Targeted Therapy
2024 Jan 22;9(1):24
Impact Factor:39.3

Materials and Methods

miR-6359-FISH was used to explore the location of miR-6359 by a **Fluorescent in Situ Hybridization Kit** (**Genepharma**; shanghai, China) following the manufacturer's instructions.

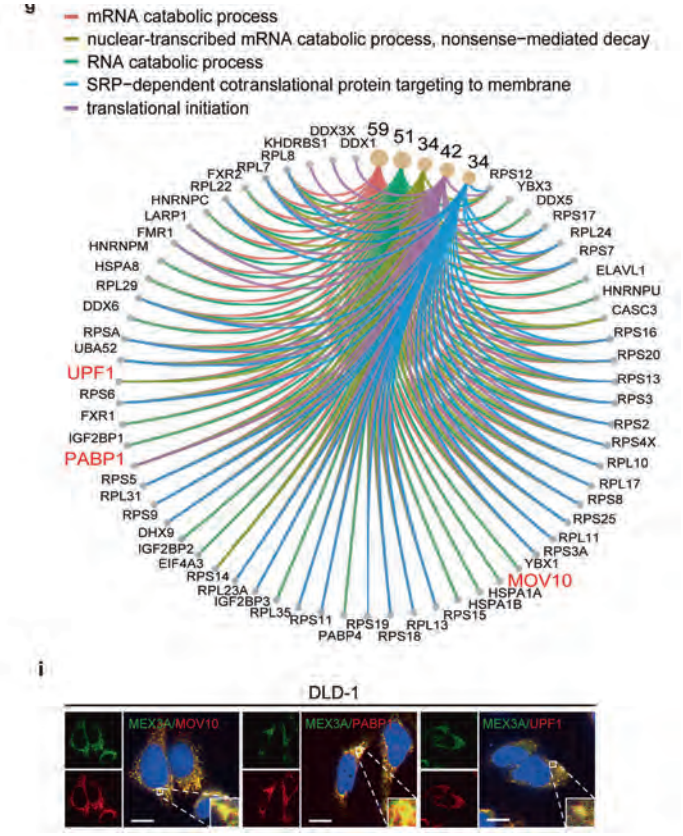
ARTICLE OPEN

Mex-3 RNA binding family member A (MEX3A)/circMPP6 complex promotes colorectal cancer progression by inhibiting autophagy

Ri-Xin Chen[1,2,3], Shui-Dan Xu[2], Min-Hua Deng[2], Shi-Hui Hao[2], Jie-Wei Chen[2,4], Xiao-Dan Ma[2], Wei-Tao Zhuang[2], Jing-Hua Cao[2], Yong-Rui Lv[2], Jin-Long Lin[2], Si-Yu Li[2], Gui-Bin Qiao[1]✉, Dan Xie[2,4]✉ and Feng-Wei Wang[2]✉

RNA-binding proteins (RBPs)-RNA networks have contributed to cancer development. Circular RNAs (circRNAs) are considered as protein recruiters; nevertheless, the patterns of circRNA-protein interactions in colorectal cancer (CRC) are still lacking. Processing bodies (PBs) formed through liquid-liquid phase separation (LLPS) are membrane-less organelles (MLOs) consisting of RBPs and RNA. Previous evidence suggests a connection between PBs dynamics and cancer progression. Despite the increasingly acknowledged crucial role of RBPs and RNA in the accumulation and maintenance of MLOs, there remains a lack of specific research on the interactions between PBs-related RBPs and circRNAs in CRC. Herein, we identify that MEX-3 RNA binding family member A (MEX3A), frequently upregulated in CRC tissues, predicts poorer patient survival. Elevated MEX3A accelerates malignance and inhibits autophagy of CRC cells. Importantly, MEX3A undergoes intrinsically disordered regions (IDRs)-dependent LLPS in the cytoplasm. Specifically, circMPP6 acts as a scaffold to facilitate the interaction between MEX3A and PBs proteins. The MEX3A/circMPP6 complex modulates PBs dynamic and promotes UPF-mediated phosphodiesterase 5A (*PDE5A*) mRNA degradation, consequently leading to the aggressive properties of CRC cells. Clinically, CRC patients exhibiting high MEX3A expression and low PDE5A expression have the poorest overall survival. Our findings reveal a collaboration between MEX3A and circMPP6 in the regulation of mRNA decay through triggering the PBs aggregation, which provides prognostic markers and/or therapeutic targets for CRC.

Signal Transduction and Targeted Therapy (2024)9:80 ; https://doi.org/10.1038/s41392-024-01787-3



Signal Transduction and Targeted Therapy
Published: 02 April 2024
Impact Factor:39.3

Materials and Methods

RNA fluorescence in situ hybridization (FISH)

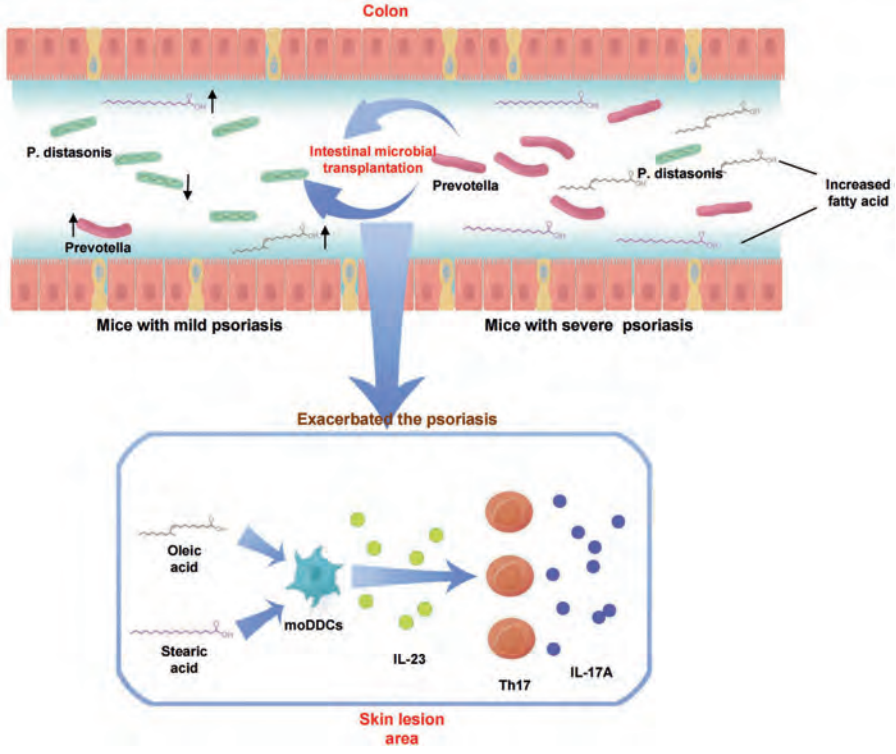
The assay was performed with **Fluorescent in Situ Hybridization Kit** (**GenePharma**, Suzhou, China, #F0539).

ARTICLE OPEN

Intestinal dysbiosis exacerbates the pathogenesis of psoriasis-like phenotype through changes in fatty acid metabolism

Qixiang Zhao[1], Jiadong Yu[1], Hong Zhou[1], Xiaoyan Wang[1], Chen Zhang[1], Jing Hu[1], Yawen Hu[1], Huaping Zheng[1], Fanlian Zeng[1], Chengcheng Yue[1], Linna Gu[1], Zhen Wang[1], Fulei Zhao[1], Pei Zhou[1], Haozhou Zhang[1], Nongyu Huang[1], Wenling Wu[1], Yifan Zhou[1] and Jiong Li[1]✉

The intestinal microbiota has been associated with host immunity as well as psoriasis; however, the mechanism of intestinal microbiota regulating psoriasis needs to be demonstrated systematically. Here, we sought to examine its role and mechanism of action in the pathogenesis of psoriasis. We found that the severity of psoriasis-like skin phenotype was accompanied by changes in the composition of the intestinal microbiota. We performed co-housing and fecal microbial transplantation (FMT) experiments using the K14-VEGF transgenic mouse model of psoriasis and demonstrated that the transfer of intestinal microbiota from mice with severe psoriasis-like skin phenotype exacerbated psoriasiform skin inflammation in mice with mild symptoms, including increasing the infiltration and differentiation of Th17, and increased the abundance of Prevotella, while decreasing that of Parabacteroides distasonis, in the colon. These alterations affected fatty acid metabolism, increasing the abundance of oleic and stearic acids. Meanwhile, gentamicin treatment significantly reduced the abundance of Prevotella and alleviated the psoriasis-like symptoms in both K14-VEGF mice and imiquimod (IMQ)-induced psoriasis-like mice. Indeed, administration of oleic and stearic acids exacerbated psoriasis-like symptoms and increased Th17 and monocyte-derived dendritic cell infiltration in the skin lesion areas in vivo, as well as increased the secretion of IL-23 by stimulating DCs in vitro. At last, we found that, treatment of PDE-4 inhibitor alleviated psoriasis-like phenotype of K14-VEGF mice accompanied by the recovery of intestinal microbiota, including the decrease of Prevotella and increase of Parabacteroides distasonis. Overall, our findings reveal that the intestinal microbiota modulates host metabolism and psoriasis-like skin inflammation in mice, suggesting a new target for the clinical diagnosis and treatment of psoriasis.



Signal Transduction and Targeted Therapy
2023 Jan 30;8(1):40
Impact Factor:39.3

Materials and Methods

Sections were pretreated with the **FISH probe reaction buffer kit** (**Genepharma**, F26501/100) and then hybridized with the probes.

Li *et al. Molecular Cancer* (2024) 23:102
https://doi.org/10.1186/s12943-024-02019-6

Molecular Cancer

RESEARCH Open Access

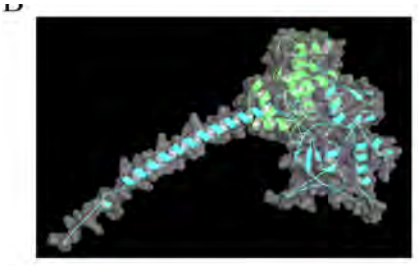
CircTRIM1 encodes TRIM1-269aa to promote chemoresistance and metastasis of TNBC via enhancing CaM-dependent MARCKS translocation and PI3K/AKT/mTOR activation

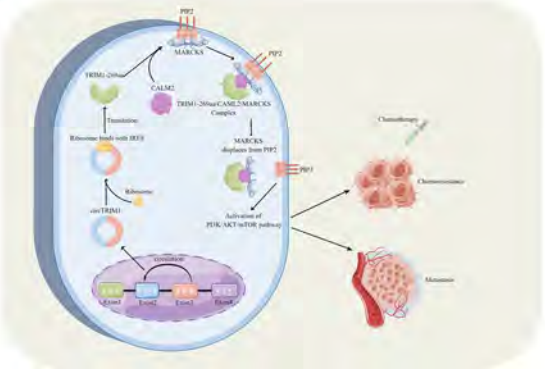
Yaming Li[1], Zekun Wang[1], Jingwen Yang[1], Yuhan Sun[1], Yinqiao He[1], Yuping Wang[2], Xi Chen[1], Yiran Liang[1], Ning Zhang[1], Xiaolong Wang[1], Wenjing Zhao[3], Guohong Hu[4*] and Qifeng Yang[1,3,5*]

Abstract

Peptides and proteins encoded by noncanonical open reading frames (ORFs) of circRNAs have recently been recognized to play important roles in disease progression, but the biological functions and mechanisms of these peptides and proteins are largely unknown. Here, we identified a potential coding circular RNA, circTRIM1, that was upregulated in doxorubicin-resistant TNBC cells by intersecting transcriptome and translatome RNA-seq data, and its expression was correlated with clinicopathological characteristics and poor prognosis in patients with TNBC. CircTRIM1 possesses a functional IRES element along with an 810 nt ORF that can be translated into a novel endogenously expressed protein termed TRIM1-269aa. Functionally, we demonstrated that TRIM1-269aa, which is involved in the biological functions of circTRIM1, promoted chemoresistance and metastasis in TNBC cells both in vitro and in vivo. In addition, we found that TRIM1-269aa can be packaged into exosomes and transmitted between TNBC cells. Mechanistically, TRIM1-269aa enhanced the interaction between MARCKS and calmodulin, thus promoting the calmodulin-dependent translocation of MARCKS, which further initiated the activation of the PI3K/AKT/mTOR pathway. Overall, circTRIM1, which encodes TRIM1-269aa, promoted TNBC chemoresistance and metastasis by enhancing MARCKS translocation and PI3K/AKT/mTOR activation. Our investigation has yielded novel insights into the roles of protein-coding circRNAs and supported circTRIM1/TRIM1-269aa as a novel promising prognostic and therapeutic target for patients with TNBC.

Keywords TNBC, circTRIM1, TRIM1-269aa, MARCKS, PI3K/AKT/mTOR





Molecular Cancer
Li et al. Molecular Cancer (2024) 23:102
Impact Factor:37.3

Materials and Methods
The FISH assay was performed using the **FISH kit** from **GenePharma**, Shanghai, China,

Zhang *et al. Molecular Cancer* (2024) 23:113
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Molecular Cancer

RESEARCH Open Access

CircPIAS1 promotes hepatocellular carcinoma progression by inhibiting ferroptosis via the miR-455-3p/NUPR1/FTH1 axis

Xiao-Yu Zhang[1,2†], Shan-Shan Li[3†], Yu-Rong Gu[1,2†], Le-Xin Xiao[1†], Xin-Yi Ma[1,2], Xin-Ru Chen[1], Jia-Liang Wang[1], Chun-Hong Liao[1], Bing-Liang Lin[1,2,4*], Yue-Hua Huang[1,2*] and Yi-Fan Lian[1*]

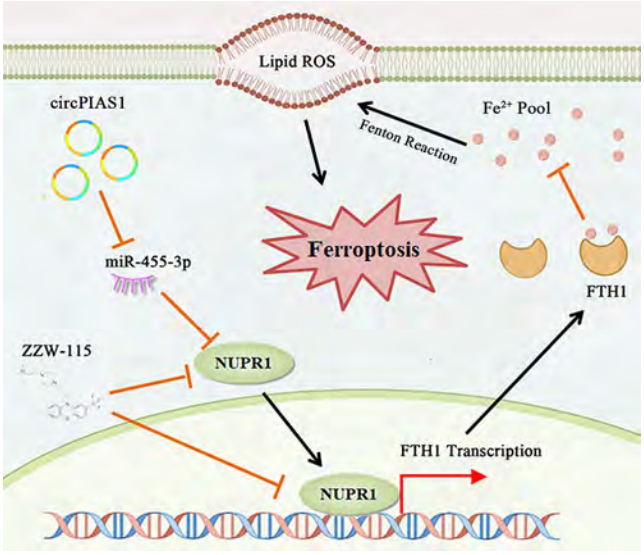
Abstract

Background The role of circRNAs in hepatocellular carcinoma (HCC) progression remains unclear. CircPIAS1 (circBase ID: hsa_circ_0007088) was identified as overexpressed in HCC cases through bioinformatics analysis. This study aimed to investigate the oncogenic properties and mechanisms of circPIAS1 in HCC development.

Methods Functional analyses were conducted to assess circPIAS1's impact on HCC cell proliferation, migration, and ferroptosis. Xenograft mouse models were employed to evaluate circPIAS1's effects on tumor growth and pulmonary metastasis in vivo. Bioinformatics analysis, RNA immunoprecipitation, and luciferase reporter assays were utilized to elucidate the molecular pathways influenced by circPIAS1. Additional techniques, including RNA pulldown, fluorescence in situ hybridization (FISH), chromatin immunoprecipitation (ChIP), qPCR, and western blotting, were used to further explore the underlying mechanisms.

Results CircPIAS1 expression was elevated in HCC tissues and cells. Silencing circPIAS1 suppressed HCC cell proliferation and migration both in vitro and in vivo. Mechanically, circPIAS1 overexpression inhibited ferroptosis by competitively binding to miR-455-3p, leading to upregulation of Nuclear Protein 1 (NUPR1). Furthermore, NUPR1 promoted FTH1 transcription, enhancing iron storage in HCC cells and conferring resistance to ferroptosis. Treatment with ZZW-115, an NUPR1 inhibitor, reversed the tumor-promoting effects of circPIAS1 and sensitized HCC cells to lenvatinib.

Conclusion This study highlights the critical role of circPIAS1 in HCC progression through modulation of ferroptosis. Targeting the circPIAS1/miR-455-3p/NUPR1/FTH1 regulatory axis may represent a promising therapeutic strategy for HCC.



Molecular Cancer
Zhang et al. Molecular Cancer (2024) 23:113
Impact Factor:37.3

Materials and Methods
The FISH assay was conducted using the **Fluorescent In Situ Hybridization Kit** (H0101, **GenePharma**, China)

Molecular Cancer

RESEARCH Open Access

A novel peptide PDHK1-241aa encoded by circPDHK1 promotes ccRCC progression via interacting with PPP1CA to inhibit AKT dephosphorylation and activate the AKT-mTOR signaling pathway

Bo Huang[1,2†], Junwu Ren[1†], Qiang Ma[1], Feifei Yang[1], Xiaojuan Pan[1], Yuying Zhang[1], Yuying Liu[1], Cong Wang[3], Dawei Zhang[3], Ling Wei[3], Lingyu Ran[4], Hongwen Zhao[4], Ce Liang[1], Xiaolin Wang[1], Shiming Wang[1], Haiping Li[1], Hao Ning[1], Ai Ran[1], Wei Li[5*], Yongquan Wang[3*] and Bin Xiao[1*]

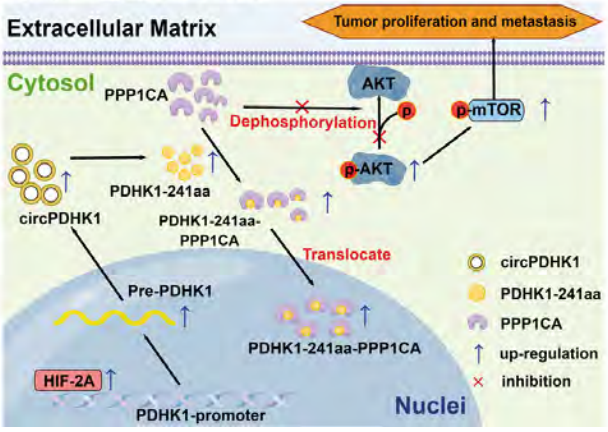
Abstract

Background Clear cell renal cell carcinoma (ccRCC) is the most prevalent kidney cancer with high aggressive phenotype and poor prognosis. Accumulating evidence suggests that circRNAs have been identified as pivotal mediators in cancers. However, the role of circRNAs in ccRCC progression remains elusive.

Methods The differentially expressed circRNAs in 4 paired human ccRCC and adjacent noncancerous tissues ccRCC were screened using circRNA microarrays and the candidate target was selected based on circRNA expression level using weighted gene correlation network analysis (WGCNA) and the gene expression omnibus (GEO) database. CircPDHK1 expression in ccRCC and adjacent noncancerous tissues ($n = 148$) were evaluated along with clinically relevant information. RT-qPCR, RNase R digestion, and actinomycin D (ActD) stability test were conducted to identify the characteristics of circPDHK1. The subcellular distribution of circPDHK1 was analyzed by subcellular fractionation assay and fluorescence in situ hybridization (FISH). Immunoprecipitation-mass spectrometry (IP-MS) and immunofluorescence (IF) were employed to evaluate the protein-coding ability of circPDHK1. ccRCC cells were transfected with siRNAs, plasmids or lentivirus approach, and cell proliferation, migration and invasion, as well as tumorigenesis and metastasis in nude mice were assessed to clarify the functional roles of circPDHK1 and its encoded peptide PDHK1-241aa. RNA-sequencing, western blot analysis, immunoprecipitation (IP) and chromatin immunoprecipitation (ChIP) assays were further employed to identify the underlying mechanisms regulated by PDHK1-241aa.

Molecular Cancer
2024 Feb 15;23(1):34
Impact Factor:37.3

Materials and Methods
Briefly, the **Cy3-labeled circP-DHK1 probe** and **FISH probe kit** were synthesized by **GenePharma** (Shanghai, China）.
The hybridization experiments were performed using a **fluorescence in situ hybridization kit** (**GenePharma,** China) according to the manufac-turer's protocol.



Molecular Cancer

RESEARCH

Open Access

Hsa_circ_0136666 stimulates gastric cancer progression and tumor immune escape by regulating the miR-375/PRKDC Axis and PD-L1 phosphorylation

Zhenyan Miao[1,2†], Jifei Li[1,2†], Yu Wang[3,4], Mingqin Shi[1,2], Xiao Gu[1,2], Xuanqi Zhang[1,2], Fang Wei[1,2], Xinying Tang[3,4*], Lufeng Zheng[1,2*] and Yingying Xing[1,2*]

Abstract

Background Targeted drugs are not quite effective for prolonging the survival of patients with gastric cancer due to off-target effects as well as tumor immune escape mechanisms. Circular RNAs widely exist in tumor regions as biomarkers and can be developed as effective drug targets.

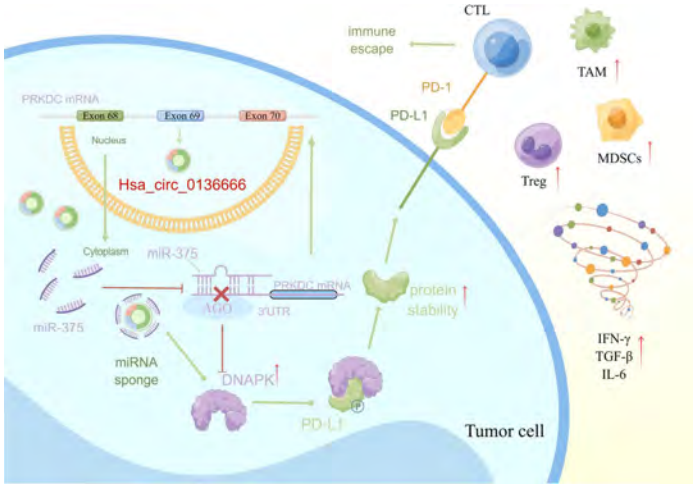
Methods Western blot, QRT-PCR, fluorescence in situ hybridization, and flow cytometry were used to investigate the function of hsa_circ_0136666 in promoting the proliferation of gastric cancer cells. Tissue immunofluorescence, enzyme-linked immunosorbent assay (ELISA), as well as flow cytometric analysis, was conducted to explore the process of tumor immune evasion in tumor-bearing mice. The differences of circRNA expression in clinical samples were analyzed through tissue microarray FISH. The effect of siRNA on improving the efficacy of anti-PDL1 drugs and suppressing the immune microenvironment was evaluated by the coadministration model.

Results We demonstrated that hsa_circ_0136666 was widely and highly expressed in gastric cancer tissues and cells. Functionally, hsa_circ_0136666 promoted gastric cancer tumor proliferation and tumor microenvironment formation, leading to tumorigenesis immune escape, and this effect was dependent on CD8 + T cells. Mechanistically, we confirmed that hsa_circ_0136666 competitively upregulated PRKDC expression by sponging miR-375-3p, regulating immune checkpoint proteins, prompting phosphorylation of PD-L1 to preventing its degradation, driving PD-L1 aggregation and suppressing immune function, thereby impairing cancer immune responses. In terms of application, we found that LNP-siRNA effectively improved anti-PDL1 drug efficacy and inhibited immune escape.

Conclusion Our results reveal an oncogenic role played by hsa_circ_0136666 in gastric cancer, driving PD-L1 phosphorylation via the miR-375/PRKDC signaling axis, prompting immune escape. This work proposes a completely new

Molecular Cancer
2023 Dec 13;22(1):205
Impact Factor:37.3

Materials and Methods
Cell slides fixed with 4% paraformaldehyde were treated with several buffers in **RNA-FISH Kit** (**GenePharma**).
MiR-375 and **PRKDC mRNA** were designed and synthesized by **GenePharma** (Shanghai, China).



Molecular Cancer

RESEARCH Open Access

TGF-β signaling promotes cervical cancer metastasis via CDR1as

Guanglei Zhong[1], Qian Zhao[1], Zhiliao Chen[1] and Tingting Yao[1,2*]

Abstract

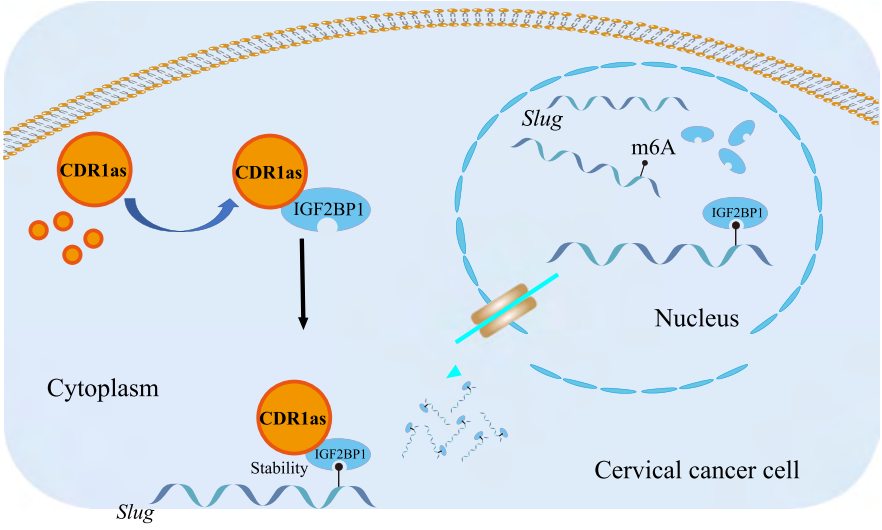
Background Due to the lack of effective treatment, metastasis is the main cause of cancer related deaths. TGF-β pathway has been reported related to cervical cancer metastasis. However, mechanism is still unclear.

Methods After agonist of TGF-β treatment, RNA sequencing revealed the expression profiles of circRNA in cervical cancer. In situ hybridization was used to analysis relationship between CDR1as and prognosis. Real-time PCR, Western blot, RNA interference, Transwell assay, Wound healing assay, RNA pulldown assay and RIP assays were performed in vitro. And in vivo cervical cancer model (including foot pad model and subcutaneous tumor formation) was also performed.

Results CDR1as was found upregulated obviously following TGF-β activation. In situ hybridization showed CDR1as was positively correlated with lymph node metastasis and shortened survival length. Simultaneously, overexpression of CDR1as promoted cervical cancer metastasis in vitro and in vivo. It was also found that CDR1as could facilitate the orchestration of IGF2BP1 on the mRNA of SLUG and stabilize it from degradation. Silencing IGF2BP1 hampers CDR1as related metastasis in cervical cancer. Additionally, effective CDR1as has been proven to activate TGF-β signaling factors known to promote EMT, including P-Smad2 and P-Smad3.

Conclusions Our study proved TGF-β signaling may promote cervical cancer metastasis via CDR1as.

Keywords Cervical cancer, Metastasis, TGF-β, CDR1as, *Slug*, IGF2BP1



Molecular Cancer
2023 Mar 31;22(1):66
Impact Factor: 37.3

Materials and Methods

To pulldown proteins with CDR1as, **biotin-labeled probes** were designed and synthesized (**GenePharma,** Suzhou, China).

Yang *et al. Molecular Cancer* (2023) 22:122
https://doi.org/10.1186/s12943-023-01814-x

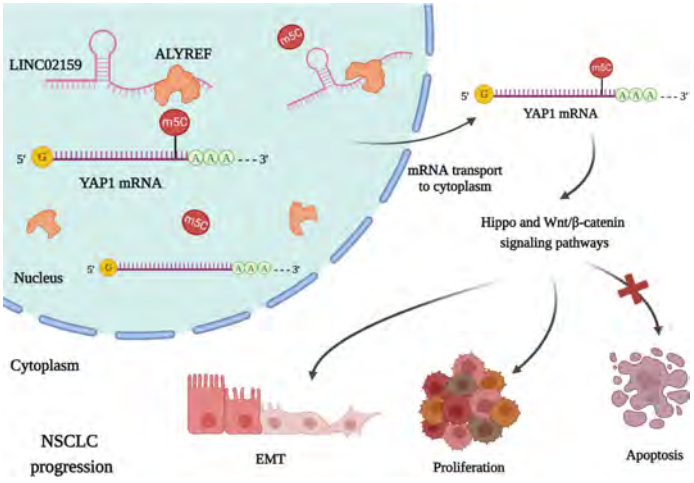
RESEARCH Open Access

LINC02159 promotes non-small cell lung cancer progression via ALYREF/YAP1 signaling

Qiurong Yang[1], Maoye Wang[1], Jing Xu[1], Dan Yu[1], Yixin Li[1], Yanke Chen[1], Xiaoxin Zhang[1], Jiahui Zhang[1], Jianmei Gu[2*] and Xu Zhang[1*]

Abstract
Lung cancer is the leading cause of cancer-related deaths worldwide. Long non-coding RNAs (lncRNAs) have emerged as key regulators of cancer development and progression, and as promising biomarkers for the diagnosis and prognosis of cancer. In this study, we identified a new lncRNA (LINC02159) that was upregulated in the tumor tissues and serum of non-small cell lung cancer (NSCLC) patients. We demonstrated that knockdown of LINC02159 inhibited NSCLC cell proliferation, migration, and invasion, but induced cell apoptosis and cell cycle arrest in vitro and retarded tumor growth in vivo, while overexpression of LINC02159 led to the opposite effect. We discovered that LINC02159 was highly correlated with cancer growth and metastasis-related pathways by using transcriptomic analysis and that YAP1 was a potential target gene of LINC02159. Mechanistically, LINC02159 bound to the Aly/REF export factor (ALYREF) to enhance the stability of YAP1 messenger RNA (mRNA) via m^5C modification, which led to the overexpression of YAP1 and the activation of the Hippo and β-catenin signaling pathways in NSCLC cells. Rescue experiments showed that LINC01259 promoted NSCLC progression in a YAP1- and ALYREF-dependent manner. In conclusion, LINC02159 plays an oncogenic role in NSCLC progression by regulating ALYREF/YAP1 signaling, and it has the potential to be utilized as a diagnostic marker and therapeutic target for NSCLC.

Keywords LncRNA, NSCLC, ALYREF, YAP1, m^5C modification, Progression



Molecular Cancer
2023 Aug 4;22(1):122
Impact Factor: 37.3

Materials and Methods

For the FISH assay, an **RNA FISH kit** (**GenePharma**) was used according to the protocol, and the **Cy3-labeled LINC02159 RNA probe** was designed and synthesized by **GenePharma**.
Specifically targeted siRNAs and **overexpression plasmids** were designed and synthesized by **GenePharma** (Suzhou, China).

Molecular Cancer

RESEARCH Open Access

CircMET promotes tumor proliferation by enhancing CDKN2A mRNA decay and upregulating SMAD3

Lei Yang[1,2†], Yi Chen[1,2†], Ning Liu[1,2], Yanwen Lu[1,2], Wenliang Ma[1,2], Zhenhao Yang[3], Weidong Gan[4*] and Dongmei Li[1,2*]

Abstract

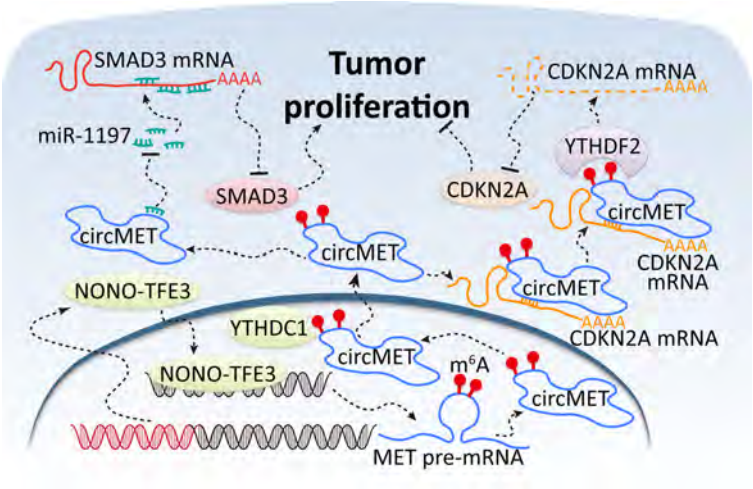
Background: Functions of CircMET (hsa_circ_0082002) which is a circular RNA and derived from MET gene remain understood incompletely. In the present study, Xp11.2 translocation/NONO-TFE3 fusion renal cell carcinoma (NONO-TFE3 tRCC) with up-regulated CircMET was employed to investigate its mechanism in cancer progression and post-transcriptional regulation.

Methods: FISH and real-time PCR were performed to explore the expression and localization circMET in NONO-TFE3 tRCC tissues and cells. The functions of circMET in tRCC were investigated by proliferation analysis, EdU staining, colony and sphere formation assay. The regulatory mechanisms among circMET, CDKN2A and SMAD3 were investi-gated by luciferase assay, RNA immunoprecipitation, RNA pulldown and targeted RNA demethylation system.

Results: The expression of circMET was upregulated by NONO-TFE3 fusion in NONO-TFE3 tRCC tissues and cells, and overexpression of circMET significantly promoted the growth of NONO-TFE3 tRCC. Mechanistic studies revealed that circMET was delivered to cytosol by YTHDC1 in N6-methyladenosine (m6A)-depend manner. CircMET enhances mRNA decay of CDKN2A by direct interaction and recruitment of YTHDF2. Meanwhile, circMET competitively absorbed miR-1197 and prevented those from SMAD3 mRNA.

Conclusions: CircMET promotes the development of NONO-TFE3 tRCC, and the regulation to both CDKN2A and SMAD3 of circMET was revealed. CircMET has the potential to serve as a novel target for the molecular therapy of NONO-TFE3 tRCC as well as the other cancer with high-expressing circMET.

Keywords: circMET, m6A modification, NONO-TFE3, CDKN2A, SMAD3



Molecular Cancer
2022 Dec;21(1):1-21
Impact Factor: 37.3

Materials and Methods

The FISH experiment was performed according to the manufacturer's instructions (**GenePharma**).

Guo et al. Molecular Cancer (2021) 20:93
https://doi.org/10.1186/s12943-021-01372-0

Molecular Cancer

RESEARCH Open Access

Circ3823 contributes to growth, metastasis and angiogenesis of colorectal cancer: involvement of miR-30c-5p/TCF7 axis

Yaxin Guo[1], Yuying Guo[2], Chen Chen[2], Dandan Fan[1], Xiaoke Wu[3], Luyang Zhao[2], Bo Shao[4], Zhenqiang Sun[4*] and Zhenyu Ji[1*]

Abstract

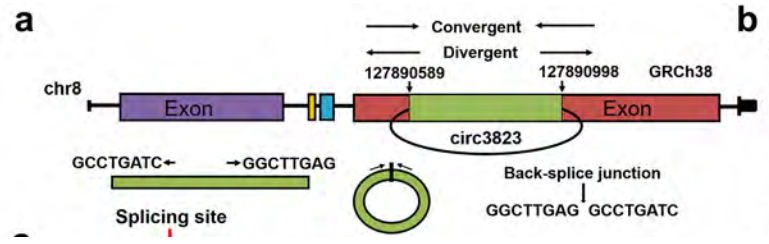
Background: Colorectal cancer (CRC) is one of the most common malignant tumours. The recurrence and metastasis of CRC seriously affect the survival rate of patients. Angiogenesis is an extremely important cause of tumour growth and metastasis. Circular RNAs (circRNAs) have been emerged as vital regulators for tumour progression. However, the regulatory role, clinical significance and underlying mechanisms still remain largely unknown.

Methods: High-throughput sequencing was used to analyse differential circRNAs expression in tumour and non-tumour tissues of CRC. In situ hybridization (ISH) and qRT-PCR were used to determine the level of circ3823 in CRC tissues and serum samples. Then, functional experiments in vitro and in vivo were performed to investigate the effects of circ3823 on tumour growth, metastasis and angiogenesis in CRC. Sanger sequencing, RNase R and Actinomycin D assay were used to verify the ring structure of circ3823. Mechanistically, dual luciferase reporter assay, fluorescent in situ hybridization (FISH), RNA immunoprecipitation (RIP) and RNA pull-down experiments were performed to confirm the underlying mechanisms of circ3823.

Results: Circ3823 was evidently highly expressed in CRC and high circ3823 expression predicted a worse prognosis of CRC patients. Receiver operating characteristic curves (ROCs) indicated that the expression of circ3823 in serum showed high sensitivity and specificity for detecting CRC which means circ3823 have the potential to be used as diagnostic biomarkers. Functional experiments in vitro and in vivo indicated that circ3823 promote CRC cell proliferation, metastasis and angiogenesis. Mechanism analysis showed that circ3823 act as a competing endogenous RNA of miR-30c-5p to relieve the repressive effect of miR-30c-5p on its target TCF7 which upregulates MYC and CCND1, and finally facilitates CRC progression. In addition, we found that N6-methyladenosine (m6A) modification exists on circ3823. And the m6A modification is involved in regulating the degradation of circ3823.

Conclusions: Our findings suggest that circ3823 promotes CRC growth, metastasis and angiogenesis through circ3823/miR-30c-5p/TCF7 axis and it may serve as a new diagnostic marker or target for treatment of CRC patients. In addition, m6A modification is involved in regulating the degradation of circ3823.

Keywords: Colorectal cancer (CRC), Tumour progression, Angiogenesis, circ3823, N6-methyladenosine (m6A)



Molecular Cancer
2021 Jun 25;20(1):93
Impact Factor: 37.3

Materials and Methods

The 5′ biotinylated miR-30c-5p pulldown probe or **NC pulldown probe** were designed and synthesized by **Gene-pharma** (Shanghai, China).

Wei et al. Molecular Cancer (2020) 19:84
https://doi.org/10.1186/s12943-020-01191-9

Molecular Cancer

RESEARCH Open Access

Circular RNA circ_0020710 drives tumor progression and immune evasion by regulating the miR-370-3p/CXCL12 axis in melanoma

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Abstract

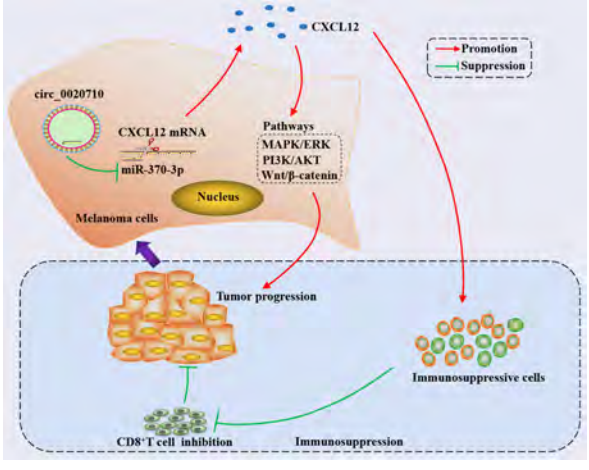
Background: Circular RNAs (circRNAs) have been reported to have critical regulatory roles in tumor biology. However, their contribution to melanoma remains largely unknown.

Methods: CircRNAs derived from oncogene CD151 were detected and verified by analyzing a large number of melanoma samples through quantitative real-time polymerase chain reaction (qRT-PCR). Melanoma cells were stably transfected with lentiviruses using circ_0020710 interference or overexpression plasmid, and then CCK-8, colony formation, wound healing, transwell invasion assays, and mouse xenograft models were employed to assess the potential role of circ_0020710. RNA immunoprecipitation, luciferase reporter assay and fluorescence in situ hybridization were used to evaluate the underlying mechanism of circ_0020710.

Results: Our findings indicated that circ_0020710 was generally overexpressed in melanoma tissues, and high level of circ_0020710 was positively correlated with malignant phenotype and poor prognosis of melanoma patients. Elevated circ_0020710 promoted melanoma cell proliferation, migration and invasion in vitro as well as tumor growth in vivo. Mechanistically, we found that high level of circ_0020710 could upregulate the CXCL12 expression via sponging miR-370-3p. CXCL12 downregulation could reverse the malignant behavior of melanoma cells conferred by circ_0020710 over expression. Moreover, we also found that elevated circ_0020710 was correlated with cytotoxic lymphocyte exhaustion, and a combination of AMD3100 (the CXCL12/CXCR4 axis inhibitor) and anti-PD-1 significantly attenuated tumor growth.

Conclusions: Elevated circ_0020710 drives tumor progression via the miR-370-3p/CXCL12 axis, and circ_0020710 is a potential target for melanoma treatment.

Keywords: circRNAs, CXCL12, Immune suppression, Melanoma



Molecular Cancer
2020 Dec;19(1):1-14
Impact Factor: 37.3

Materials and Methods

Cy3-labeled circMET probes were synthesized by **GenePharma** Technology (Shanghai, China). FISH was performed using a **FISH kit** (**GenePharma**) according to the manufacturer's instructions.

Luo et al. Molecular Cancer (2020) 19:86
https://doi.org/10.1186/s12943-020-01203-8

Molecular Cancer

RESEARCH Open Access

Circular RNA circCCDC9 acts as a miR-6792-3p sponge to suppress the progression of gastric cancer through regulating CAV1 expression

Zai Luo[1†], Zeyin Rong[1†], Jianming Zhang[1†], Zhonglin Zhu[1,2†], Zhilong Yu[1], Tengfei Li[1], Zhongmao Fu[1], Zhengjun Qiu[1] and Chen Huang[1*]

Abstract

Background: As a novel type of noncoding RNAs, covalently closed circular RNAs (circRNAs) are ubiquitously expressed in eukaryotes. Emerging studies have related dysregulation of circRNAs to tumorigenesis. However, the biogenesis, regulation, function and mechanism of circRNAs in gastric cancer (GC) remain largely unclear.

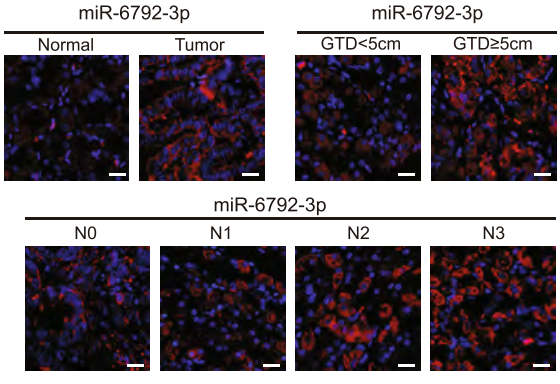
Methods: The expression profile of circRNAs in 6 pairs of GC tissues and adjacent non-tumor tissues was analyzed by RNA-sequencing. Quantitative real-time PCR was used to determine the expression level of circCCDC9 in GC tissues and cell lines. Then, functional experiments in vitro and in vivo were employed to explore the effects of circCCDC9 on tumor growth and metastasis in GC. Mechanistically, dual luciferase reporter, fluorescence in situ hybridization (FISH), RNA immunoprecipitation (RIP) and RNA pull-down assays were performed to confirm that circCCDC9 directly sponged miR-6792-3p and alleviated suppression on target CAV1 expression.

Results: Evidently down-regulated expression of circCCDC9 was observed in both GC tissues and cell lines. Expression of circCCDC9 was negatively correlated with tumor size, lymph node invasion, advanced clinical stage and overall survival in GC patients. Functionally, overexpression of circCCDC9 significantly inhibited the proliferation, migration and invasion of GC cell lines in vitro and tumor growth and metastasis in vivo, whereas miR-6792-3p mimics counteracted these effects. Mechanistic analysis demonstrated that circCCDC9 acted as a “ceRNA” of miR-6792-3p to relieve the repressive effect of miR-6792-3p on its target CAV1, then suppressed the tumorigenesis of GC.

Molecular Cancer
2020 May 9; 19:86
Impact Factor: 37.3

Materials and Methods

Cy3-labeled circCCDC9 probes and **FAM-labeled miR-6792-3p** were designed and synthesized by **GenePharma** (Shanghai,China).



Li et al. Molecular Cancer (2020) 19:142
https://doi.org/10.1186/s12943-020-01259-6

Molecular Cancer

RESEARCH Open Access

Circular HER2 RNA positive triple negative breast cancer is sensitive to Pertuzumab

Jie Li[1,2†], Maoguang Ma[1,2†], Xuesong Yang[1†], Maolei Zhang[1,3†], Jingyan Luo[4], Huangkai Zhou[1,3], Nunu Huang[1,3], Feizhe Xiao[5], Bingquan Lai[4], Weiming Lv[2] and Nu Zhang[1,3*]

Abstract

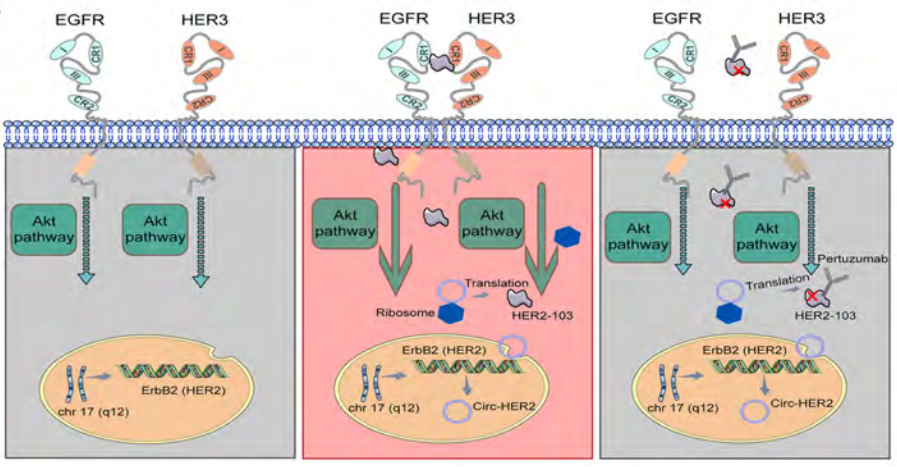
Background: Triple negative breast cancer (TNBC) remains the most challenging breast cancer subtype so far. Specific therapeutic approaches have rarely achieved clinical improvements in treatment of TNBC patients and effective molecular biomarkers are largely unknown.

Methods: We used paired TNBC samples and high throughput RNA sequencing to identify differentially expressed circRNAs. Sucrose gradient polysome fractionation assay, antibody and Mass spectra were used to validate active circRNA translation. The novel protein function was validated in vitro and in vivo by gain or loss of function assays. Mechanistic results were concluded by immunoprecipitation analyses and kinase activity assay.

Results: Circular HER2 RNA (circ-HER2) encoded a novel protein, HER2–103. Unexpectedly, while HER2 mRNA and protein were barely detected, circ-HER2/HER2–103 was expressed in ~ 30% TNBC clinical samples. Circ-HER2/HER2–103 positive TNBC patients harbored worse overall prognosis than circ-HER2/HER2–103 negative patients. Knockdown circ-HER2 inhibited TNBC cells proliferation, invasion and tumorigenesis in vitro and in vivo, suggesting the critical role of circ-HER2/HER2–103 in TNBC tumorigenicity. Mechanistically, HER2–103 promoted homo/hetero dimerization of epidermal growth factor receptor (EGFR)/HER3, sustained AKT phosphorylation and downstream malignant phenotypes. Furthermore, HER2–103 shared most of the same amino acid sequences as HER2 CR1 domain which could be antagonized by Pertuzumab, a clinical used HER2 antibody. Pertuzumab markedly attenuated in vivo tumorigenicity of circ-HER2/HER2–103 expressing TNBC cells but showed no effects in circ-HER2/HER2–103 negative TNBC cells.

Molecular Cancer
2020 Sep 11; 19:142
Impact Factor: 37.3

Materials and Methods
RNA FISH assay was performed using **RNA FISH kit** (Suzhou **GenePharma** Co, Ltd., Suzhou, China).



Zhang et al. Molecular Cancer (2020) 19:110
https://doi.org/10.1186/s12943-020-01222-5

Molecular Cancer

RESEARCH Open Access

Cancer cell-derived exosomal circUHRF1 induces natural killer cell exhaustion and may cause resistance to anti-PD1 therapy in hepatocellular carcinoma

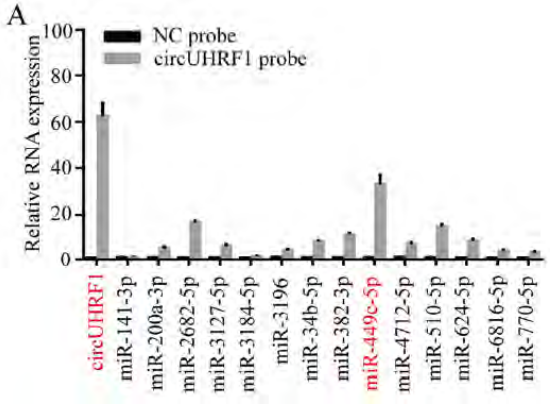
Peng-Fei Zhang[1,2,3†], Chao Gao[1,2†], Xiao-Yong Huang[1,2†], Jia-Cheng Lu[1,2†], Xiao-Jun Guo[1,2], Guo-Ming Shi[1,2*], Jia-Bin Cai[1,2*] and Ai-Wu Ke[1,2*]

Abstract

Objective: Natural killer (NK) cells play a critical role in the innate antitumor immune response. Recently, NK cell dysfunction has been verified in various malignant tumors, including hepatocellular carcinoma (HCC). However, the molecular biological mechanisms of NK cell dysfunction in human HCC are still obscure.

Methods: The expression of circular ubiquitin-like with PHD and ring finger domain 1 RNA (circUHRF1) in HCC tissues, exosomes, and cell lines was detected by qRT-PCR. Exosomes were isolated from the culture medium of HCC cells and plasma of HCC patients using an ultracentrifugation method and the ExoQuick Exosome Precipitation Solution kit and then characterized by transmission electronic microscopy, NanoSight and western blotting. The role of circUHRF1 in NK cell dysfunction was assessed by ELISA. In vivo circRNA precipitation, RNA immunoprecipitation, and luciferase reporter assays were performed to explore the molecular mechanisms of circUHRF1 in NK cells. In a retrospective study, the clinical characteristics and prognostic significance of circUHRF1 were determined in HCC tissues.

Results: Here, we report that the expression of circUHRF1 is higher in human HCC tissues than in matched adjacent nontumor tissues. Increased levels of circUHRF1 indicate poor clinical prognosis and NK cell dysfunction in patients with HCC. In HCC patient plasma, circUHRF1 is predominantly secreted by HCC cells in an exosomal manner, and circUHRF1 inhibits NK cell-derived IFN-γ and TNF-α secretion. A high level of plasma exosomal circUHRF1 is associated with a decreased NK cell proportion and decreased NK cell tumor infiltration. Moreover, circUHRF1 inhibits NK cell function by upregulating the expression of TIM-3 via degradation of miR-449c-5p. Finally, we show that circUHRF1 may drive resistance to anti-PD1 immunotherapy in HCC patients.



Molecular Cancer
2020 Jun 27 ; 19: 110
Impact Factor: 37.3

Materials and Methods

The **biotinylated circUHRF1 probe, biotinylated circRAN-RIL probe**, and **biotinylated negative control (NC) probe** (**GenePharma**, China).

Zhang et al. Molecular Cancer (2020) 19:110
https://doi.org/10.1186/s12943-020-01222-5

Molecular Cancer

RESEARCH Open Access

Cancer cell-derived exosomal circUHRF1 induces natural killer cell exhaustion and may cause resistance to anti-PD1 therapy in hepatocellular carcinoma

Peng-Fei Zhang[1,2,3†], Chao Gao[1,2†], Xiao-Yong Huang[1,2†], Jia-Cheng Lu[1,2†], Xiao-Jun Guo[1,2], Guo-Ming Shi[1,2*], Jia-Bin Cai[1,2*] and Ai-Wu Ke[1,2*]

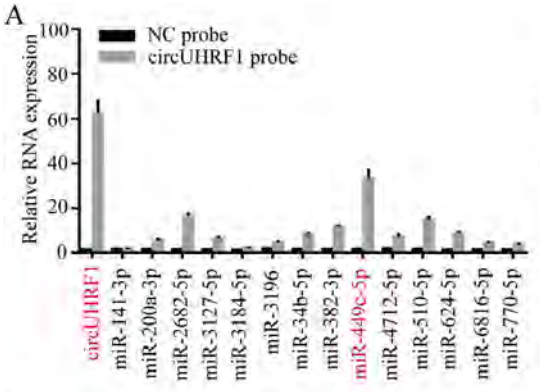
Abstract

Objective: Natural killer (NK) cells play a critical role in the innate antitumor immune response. Recently, NK cell dysfunction has been verified in various malignant tumors, including hepatocellular carcinoma (HCC). However, the molecular biological mechanisms of NK cell dysfunction in human HCC are still obscure.

Methods: The expression of circular ubiquitin-like with PHD and ring finger domain 1 RNA (circUHRF1) in HCC tissues, exosomes, and cell lines was detected by qRT-PCR. Exosomes were isolated from the culture medium of HCC cells and plasma of HCC patients using an ultracentrifugation method and the ExoQuick Exosome Precipitation Solution kit and then characterized by transmission electronic microscopy, NanoSight and western blotting. The role of circUHRF1 in NK cell dysfunction was assessed by ELISA. In vivo circRNA precipitation, RNA immunoprecipitation, and luciferase reporter assays were performed to explore the molecular mechanisms of circUHRF1 in NK cells. In a retrospective study, the clinical characteristics and prognostic significance of circUHRF1 were determined in HCC tissues.

Results: Here, we report that the expression of circUHRF1 is higher in human HCC tissues than in matched adjacent nontumor tissues. Increased levels of circUHRF1 indicate poor clinical prognosis and NK cell dysfunction in patients with HCC. In HCC patient plasma, circUHRF1 is predominantly secreted by HCC cells in an exosomal manner, and circUHRF1 inhibits NK cell-derived IFN-γ and TNF-α secretion. A high level of plasma exosomal circUHRF1 is associated with a decreased NK cell proportion and decreased NK cell tumor infiltration. Moreover, circUHRF1 inhibits NK cell function by upregulating the expression of TIM-3 via degradation of miR-449c-5p. Finally, we show that circUHRF1 may drive resistance to anti-PD1 immunotherapy in HCC patients.

Conclusions: Exosomal circUHRF1 is predominantly secreted by HCC cells and contributes to immunosuppression by inducing NK cell dysfunction in HCC. CircUHRF1 may drive resistance to anti-PD1 immunotherapy, providing a potential therapeutic strategy for patients with HCC.



Molecular Cancer
2020 Jun 27;19:110
Impact Factor: 37.3

Materials and Methods

In brief, to generate probe-coated beads, **the biotinylated circUHRF1 probe**, **biotinylated circAN-RIL probe**, and **biotinylated negative control (NC) probe** (**GenePharma**, China).

Bi et al. Molecular Cancer (2019) 18:133
https://doi.org/10.1186/s12943-019-1060-9

Molecular Cancer

RESEARCH Open Access

Circular RNA circ-*ZKSCAN1* inhibits bladder cancer progression through miR-1178-3p/p21 axis and acts as a prognostic factor of recurrence

Junming Bi[1,2†], Hongwei Liu[3†], Wei Dong[4†], Weibin Xie[1,2†], Qingqing He[1,2], Zijian Cai[1,2], Jian Huang[1,2*] and Tianxin Lin[1,2*]

Abstract

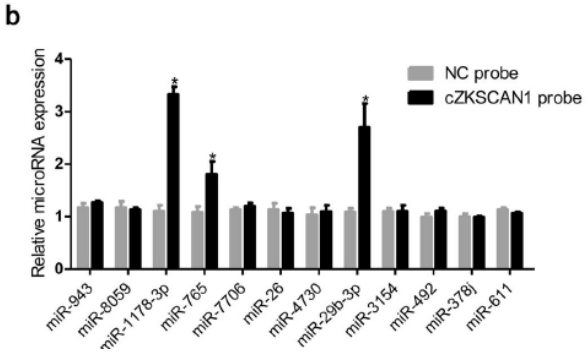
Background: Circular RNAs (circRNAs) represent a subclass of regulatory RNAs that have been shown to have significant regulatory roles in cancer progression. However, the biological functions of circRNAs in bladder cancer (BCa) are largely unknown.

Methods: Cell invasion models were established, and invasion-related circRNAs were detected by qPCR. Using above method, circ-ZKSCAN1 was picked out for further study. Circ-ZKSCAN1 expression and survival analyses were performed through qPCR. The survival curves were generated by the Kaplan-Meier method, and the log-rank test was used to assess the significance. Cell proliferation, migration and invasion were examined to investigate the function of circ-ZKSCAN1. Tumorigenesis in nude mice was assessed to determine the effect of circ-ZKSCAN1 in bladder cancer. Biotin-coupled probe pull-down assays, FISH and luciferase reporter assays were conducted to confirm the relationship between circ-ZKSCAN1 and microRNA. RNA-seq revealed different molecular changes in downstream genes.

Results: Here, we found that circ-ZKSCAN1 was downregulated in BCa tissues and cell lines. Circ-ZKSCAN1 levels were associated with survival, tumor grade, pathological T stage and tumor recurrence. Overexpressed circ-ZKSCAN1 inhibits cell proliferation, migration, invasion and metastasis in vitro and in vivo. Mechanistically, we demonstrated that circ-ZKSCAN1 upregulated p21 expression by sponging miR-1178-3p, which suppressed the aggressive biological behaviors in bladder cancer.

Molecular Cancer
2019 Sep 3 ; 18: 133
Impact Factor: 37.3

Materials and Methods
Circ-ZKSCAN1 biotinylated-probe was designed and syny-hesized by **GenePharma** (Shanghai, China).
Cells were incubate with **cy3-labelled circ-ZKSCAN1 probe** (**GenePharma**, China).



Lu et al. Molecular Cancer (2019) 18:111
https://doi.org/10.1186/s12943-019-1040-0

Molecular Cancer

RESEARCH Open Access

Circular RNA circSLC8A1 acts as a sponge of miR-130b/miR-494 in suppressing bladder cancer progression via regulating PTEN

Qun Lu[1†], Tianyao Liu[1†], Huijin Feng[2†], Rong Yang[1], Xiaozhi Zhao[1], Wei Chen[1], Bo Jiang[1], Haixiang Qin[1], Xu Guo[2], Minghui Liu[2], Limin Li[2] and Hongqian Guo[1*]

Abstract

Background: Circular RNAs (circRNAs) are a novel class of endogenous noncoding RNAs formed by a covalently closed loop, and increasing evidence has revealed that circRNAs play crucial functions in regulating gene expression. CircSLC8A1 is a circRNA generated from the SLC8A1 gene. Currently, the role and underlying molecular mechanisms of circSLC8A1 in bladder cancer remain unknown.

Methods: The differentially expressed circRNAs were identified from RNA-sequencing data, and circSLC8A1 was determined as a new candidate circRNA. qRT-PCR was used to detect the expression of circRNAs, miRNAs and mRNAs in human tissues and cells. RNA pull-down assay and luciferase reporter assay were used to investigate the interactions between the specific circRNA, miRNA and mRNA. The effects of circSLC8A1 on bladder cancer cells were explored by transfecting with plasmids in vitro and in vivo. The expression of PTEN was detected by Western blot. The biological roles were measured by wound healing assay, transwell assay, and CCK-8 assay.

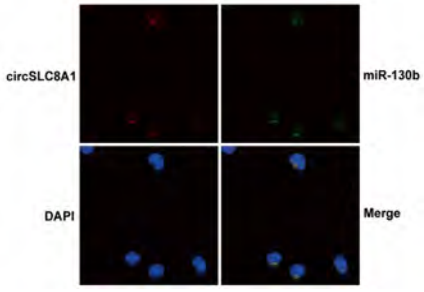
Results: In the present study, we found that circSLC8A1 was down-regulated in bladder cancer tissues and cell lines, and circSLC8A1 expression was associated with the pathological stage and histological grade of bladder cancer. Over-expression of circSLC8A1 inhibited cell migration, invasion and proliferation both in vitro and in vivo. Mechanistically, circSLC8A1 could directly interact with miR-130b/miR-494, and subsequently act as a miRNA sponge to regulate the expression of the miR-130b/miR-494 target gene PTEN and downstream signaling pathway, which suppressed the progression of bladder cancer.

Conclusions: CircSLC8A1 acts as a tumor suppressor by a novel circSLC8A1/miR-130b, miR-494/PTEN axis, which may provide a potential biomarker and therapeutic target for the management of bladder cancer.

Molecular Cancer
2019 Jun 22;18(1):111
Impact Factor: 37.3

Materials and Methods

The **probes** were designed and synthesized by **Genepharma** (Shanghai, China), and the signals of the probes were detected by a **Fluorescent In Situ Hybridization Kit** (**Genepharma**, Shanghai, China) according to the manufacturer' s instructions.



Dong et al. Molecular Cancer (2019) 18:95
https://doi.org/10.1186/s12943-019-1025-z

Molecular Cancer

RESEARCH Open Access

Circular RNA ACVR2A suppresses bladder cancer cells proliferation and metastasis through miR-626/EYA4 axis

Wei Dong[1,2†], Junming Bi[1,2†], Hongwei Liu[1,2†], Dong Yan[1,2], Qingqing He[1,2], Qianghua Zhou[1,2], Qiong Wang[1,2], Ruihui Xie[1,2], Yinjie Su[1,2], Meihua Yang[1,2], Tianxin Lin[1,2*] and Jian Huang[1,2*]

Abstract

Background: Circular RNAs (circRNAs) have been considered to mediate occurrence and development of human cancers, generally acting as microRNA (miRNA) sponges to regulate downstream genes expression. However, the aberrant expression profile and dysfunction of circRNAs in human bladder cancer remain to be investigated. The present study aims to elucidate the potential role and molecular mechanism of circACVR2A in regulating the proliferation and metastasis of bladder cancer.

Methods: circACVR2A (hsa_circ_0001073) was identified by RNA-sequencing and validated by quantitative real-time polymerase chain reaction and agarose gel electrophoresis. The role of circACVR2A in bladder cancer was assessed both in vitro and in vivo. Biotin-coupled probe pull down assay, biotin-coupled microRNA capture, dual-luciferase reporter assay, and fluorescence in situ hybridization were conducted to evaluate the interaction between circACVR2A and microRNAs.

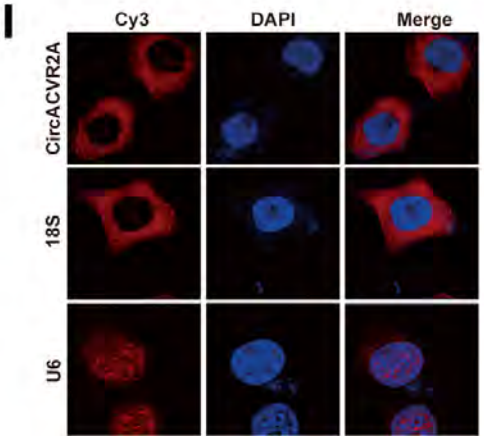
Results: The expression of circACVR2A was lower in bladder cancer tissues and cell lines. The down-regulation of circACVR2A was positively correlated with aggressive clinicopathological characteristics, and circACVR2A served as an independent risk factor for overall survival in bladder cancer patients after cystectomy. Our in vivo and in vitro data indicated that circACVR2A suppressed the proliferation, migration and invasion of bladder cancer cells. Mechanistically, we found that circACVR2A could directly interact with miR-626 and act as a miRNA sponge to regulate EYA4 expression.

Molecular Cancer
2019 May 17; 18: 95
Impact Factor: 37.3

Materials and Methods

The biotinylated **circACVR2A probe** and **oligo probe** (**GenePharma**, China) the **Cy3-labeled circACVR2A probe** and **Cy5-labeled miRNA-626 probe** were designed and synthesized by **GenePharma** (Shanghai, China).

The signals of the probe were detected by the **Fluorescent In Situ Hybridization Kit** (**GenePharma**, China).



Liu et al. Molecular Cancer (2018) 17:161
https://doi.org/10.1186/s12943-018-0908-8

Molecular Cancer

RESEARCH Open Access

Invasion-related circular RNA circFNDC3B inhibits bladder cancer progression through the miR-1178-3p/G3BP2/SRC/FAK axis

Hongwei Liu†, Junming Bi†, Wei Dong†, Meihua Yang, Juanyi Shi, Ning Jiang, Tianxin Lin* and Jian Huang*

Abstract

Background: Increasing evidence has revealed that circular RNAs (circRNAs) play crucial roles in cancer biology. However, the role and underlying regulatory mechanisms of circFNDC3B in bladder cancer (BC) remain unknown. Methods: A cell invasion model was established by repeated transwell assays, and invasion-related circRNAs in BC were identified through an invasion model. The expression of circFNDC3B was detected in 82 BC tissues and cell lines by quantitative real-time PCR. Functional assays were performed to evaluate the effects of circFNDC3B on proliferation, migration and invasion in vitro-, and on tumorigenesis and metastasis in vivo. The relationship between circFNDC3B and miR-1178-3p was confirmed by fluorescence in situ hybridization, pull-down assay and luciferase reporter assay.

Results: In the present study, we identified a novel circRNA (circFNDC3B) through our established BC cell invasion model. We found that circFNDC3B was dramatically downregulated in BC tissues and correlated with pathological T stage, grade, lymphatic invasion and patients' overall survival rate. Functionally, overexpression of circFNDC3B significantly inhibited proliferation, migration and invasion both in vitro and in vivo. Mechanistically, circFNDC3B could directly bind to miR-1178-3p, which targeted the 5′ UTR of the oncogene G3BP2. Moreover, circFNDC3B acted as a miR-1178-3p sponge to suppress G3BP2, thereby inhibiting the downstream SRC/FAK signaling pathway.

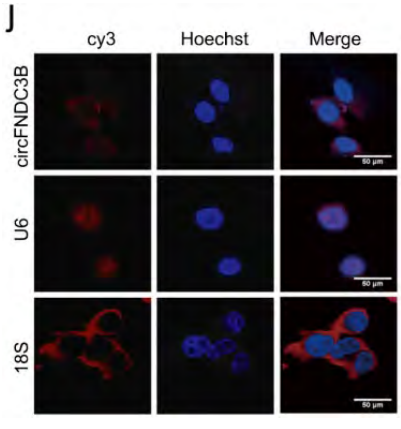
Conclusions: CircFNDC3B may serve as a novel tumor suppressive factor and potential target for new therapies in human BC.

Keywords: circFNDC3B, miR-1178-3p, G3BP2, SRC/FAK, Bladder cancer

Molecular Cancer
2018 Nov 20;17(1):161
Impact Factor: 37.3

Materials and Methods

The signals of the probe were detected by a **Fluorescent In Situ Hybridization Kit** (**GenePharma**, China) according to the manufacturer's protocol. For miR-188-3p mimics delivery, chemically modified mimics were 2'-OMe modified (GenePharma, Shanghai).



Tang *et al. Molecular Cancer* (2025) 24:165
https://doi.org/10.1186/s12943-025-02341-7

Molecular Cancer

RESEARCH Open Access

The EGR1-mediated lncRNA TENM3-AS1 potentiates gastric cancer metastasis via reprogramming fatty acid metabolism

Yuhui Tang[1†], Baiwei Zhao[1†], Wanchuan Wang[2†], Haoming Chen[3], Junsheng Zhang[1], Yi Xie[1], Yongming Chen[1], Feizhi Lin[1], Yuanfang Li[1*], Xiaohui Zhai[4*] and Wen Zhou[2*]

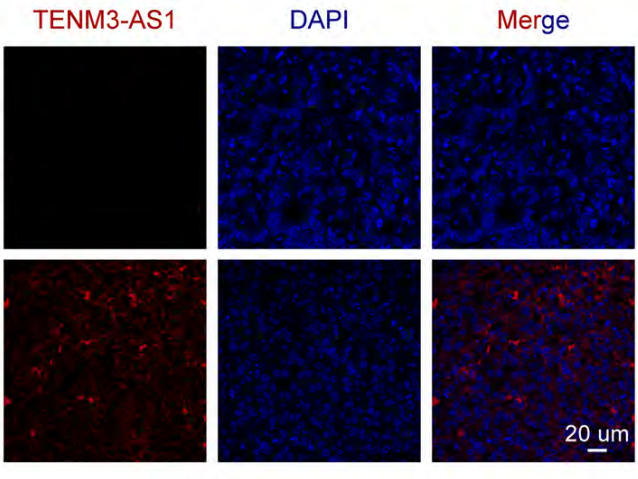
Abstract

Background Long non-coding RNAs (lncRNAs) are essential modulators in tumor progression. While fatty acid (FA) metabolism can potentiate tumorigenesis, colonization, and metastasis, the roles of lncRNAs in reprograming FA metabolism and regulating gastric cancer (GC) metastasis remain elusive.

Methods Whole RNA-sequencing and in silico analyses were conducted to identify clinically significant lncRNAs involved in GC metastasis. Among the identified lncRNAs, we focused on the novel lncRNA TENM3-AS1. RT-qPCR and FISH analyses revealed an increased expression of TENM3-AS1 in GC cell lines and patients. In vitro and in vivo functional experiments validated the effects of TENM3-AS1 to GC metastasis and the reprogramming of FA metabolism. ChIP, Biotinylated RNA pull-down, RIP, CHX-chase assay, ubiquitination assay, and RNA stabilization assay were employed to perceive the mechanisms underlying the effects of TENM3-AS1 in GC cells.

Results TENM3-AS1 expression was significantly elevated in metastatic tumors and advanced primary tumors of GC patients. This increased expression was also associated with a worsened overall survival and progression-free survival. Functionally, TENM3-AS1 enhanced the migration and invasiveness of GC cells in vitro, promoted tumorigenesis and liver metastasis in vivo, and increased FA biosynthesis in GC cells. Mechanistically, our studies showed that the transcription factor EGR1 activated TENM3-AS1, which in turn upregulated the expression of FASN and hnRNPK. Furthermore, TENM3-AS1 interacted with and stabilized hnRNPK by increasing its deubiquitination. This interaction reprogrammed FA metabolism and promoted GC progression by increasing FASN mRNA stability through hnRNPK.

Conclusions In this study, by comparing lncRNA sequencing data from paired primary and peritoneal metastatic tumors and public transcriptome data from non-metastatic and metastatic samples, we clarified a novel lncRNA,



Molecular Cancer
(2025) 24:165
Impact Factor: 33.9

Materials and Methods
Fluorescent In Situ Hybridization Kit
(**GenePharma**, Shanghai, China)

Situ *et al. Molecular Cancer* (2026) 25:13
https://doi.org/10.1186/s12943-025-02530-4

Molecular Cancer

RESEARCH Open Access

CircRNF10 sequestrates β-catenin by a dual regulatory circuit of direct degradation and a miR-1275/DKK3-mediated inhibition in driver gene- negative lung adenocarcinoma

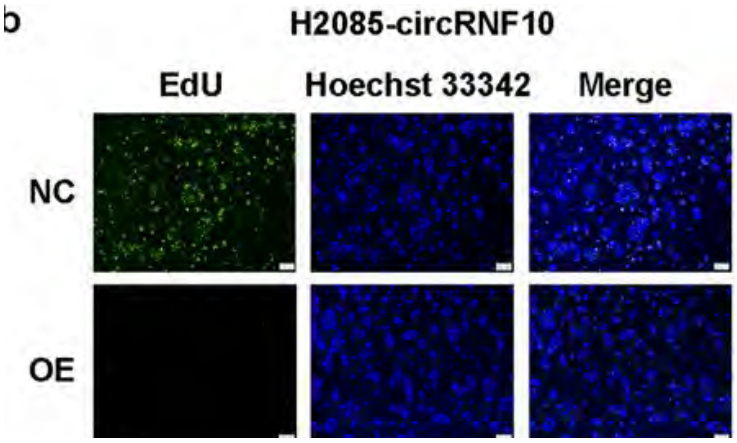
Xiaohua Situ[1,2†], Xinwei Wang[1,2†], Xiting Liao[1,2†], Xiaoxuan Zhang[1,2], Sicheng Chen[1,3], Fei Fang[1,2], Lihong Wei[1,2], Peng Wu[1,2], Zhiyu Liu[4], Honglei Chen[5], Kejing Tang[3*], Lihong Bai[3,6*] and Zunfu Ke[1,2*]

Abstract

Background Circular RNAs (circRNAs) exert critical regulatory functions in tumor biology by modulating pathways associated with oncogenesis or tumor suppression. Despite substantial progress in elucidating their roles in several malignancies, the contribution of circRNAs to the pathogenesis of driver gene-negative lung adenocarcinoma (LUAD), a molecular subtype lacking actionable genetic alterations and exhibiting limited response to existing targeted or immunotherapeutic strategies, remains poorly defined.

Methods The expression of circRNF10 in driver gene-negative LUAD was analyzed using circRNA microarray analysis followed by RT-qPCR validation. A series of functional assays were performed both in vitro and in vivo to evaluate the effects of circRNF10 on tumor cell behavior, including proliferation (EdU incorporation), migration (wound healing), and invasion (transwell assays), as well as tumor growth in a murine model. To elucidate the underlying molecular mechanism, we employed a combination of computational and experimental approaches, including AlphaFold3-based structural prediction, in vitro transcription, biotin-labeled RNA pulldown, RNA immunoprecipitation (RIP), and dual-luciferase reporter assays.

Results In this study, we identified a previously uncharacterized circular RNA, circRNF10, which is markedly downregulated in driver gene-negative lung adenocarcinoma (LUAD) and positively associated with favorable clinical outcomes. Functional analyses revealed that circRNF10 overexpression suppresses LUAD cell proliferation, migration, and invasion in vitro and in vivo, primarily through inhibition of the Wnt/β-catenin signaling pathway. Mechanistically,



Molecular Cancer
(2026) 25:13
Impact Factor: 33.9

Materials and Methods
The **probes with FAM- or Cy3-labelled circRNF10** and **Cy3-labelled miR-1275** were synthesized by **GenePharma** (China).

Molecular Cancer

RESEARCH Open Access

CircABCA1 promotes ccRCC by reprogramming cholesterol metabolism and facilitating M2 macrophage polarization through IGF2BP3-mediated stabilization of SCARB1 mRNA

Hao Ning[1,2†], Yan Jiang[2†], Binbin Li[2], Junwu Ren[2], Cong Wang[3], Ling Wei[3], Linfei Li[3], Ai Ran[2], Zuozhang Li[2], Jiao Li[2], Wei Li[4*], Yongquan Wang[3*] and Bin Xiao[2*]

Abstract

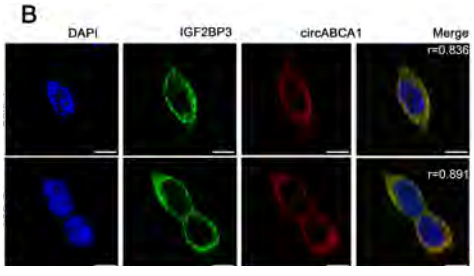
Background The reliance of clear cell renal cell carcinoma (ccRCC) on exogenous cholesterol import implies a metabolic susceptibility. This susceptibility represents a potential avenue that can be exploited as a novel therapeutic approach for ccRCC. Circular RNAs (circRNAs) are emerging regulators in cancer, yet their roles in ccRCC lipid metabolism and tumor microenvironment remodeling remain unclear. This study investigates the tumor-promoting role of circABCA1 in ccRCC cholesterol homeostasis and M2 macrophage polarization.

Methods The expression levels of circABCA1, IGF2BP3, SCARB1, autophagy-related proteins, and the IGF1R/PI3K/AKT/mTOR and ABCA1/ABCG1 pathways were measured using RT-qPCR and western blot. Untargeted metabolomics, RNA- sequencing, and MS2 RNA-pulldown were conducted to identify targets. Interaction analyses included RNA immunoprecipitation, RNA pull-down, and RNA fluorescence in situ hybridization (FISH) assays. Lipid raft measurements, cholesterol uptake/efflux assays, and lipophagy assessments were performed. A co-culture system between M2 macrophages and ccRCC cells was established. In vivo tumorigenesis and metastasis were evaluated using xenograft models and a hepatic metastasis model. Statistical analyses involved Student's t-tests and ANOVA; significance set at $P < 0.05$.

Results We identified a novel lipid metabolism-related circRNA, circABCA1, which was upregulated in ccRCC and positively correlated with tumor stage and distant metastasis. Functionally, circABCA1 enhanced the half-life of SCARB1 mRNA by forming a circABCA1-IGF2BP3-SCARB1 mRNA ternary complex, thereby increasing the expression of SCARB1 and consequent cholesterol uptake. Next, elevated cholesterol caused by circABCA1-SCARB1 axis-maintained lipid rafts, initiated IGF1R/PI3K/AKT/mTOR cascade, and protected lipid droplets from being destructed

Molecular Cancer
(2025) 24:199
Impact Factor: 33.5

Materials and Methods
Cy3-labeled circABCA1 probes and the **FISH kit**
were synthesized by **GenePharma**



Journal of Hematology & Oncology

RESEARCH Open Access

Low expression of TRAF3IP2-AS1 promotes progression of *NONO-TFE3* translocation renal cell carcinoma by stimulating N^6-methyladenosine of PARP1 mRNA and downregulating PTEN

Lei Yang[1,2], Yi Chen[1,2], Ning Liu[1,2], QianCheng Shi[1,2], Xiaodong Han[1,2], Weidong Gan[3*] and Dongmei Li[1,2*]

Abstract

Background: NONO-TFE3 translocation renal cell carcinoma (NONO-TFE3 tRCC) is one subtype of RCCs associated with Xp11.2 translocation/TFE3 gene fusions RCC (Xp11.2 tRCCs). Long non-coding RNA (lncRNA) has attracted great attention in cancer research. The function and mechanisms of TRAF3IP2 antisense RNA 1 (TRAF3IP2-AS1), a natural antisense lncRNA, in NONO-TFE3 tRCC remain poorly understood.

Methods: FISH and qRT-PCR were undertaken to study the expression, localization and clinical significance of TRAF3IP2-AS1 in Xp11.2 tRCC tissues and cells. The functions of TRAF3IP2-AS1 in tRCC were investigated by prolifera-tion analysis, EdU staining, colony and sphere formation assay, Transwell assay and apoptosis analysis. The regulatory mechanisms among TRAF3IP2-AS1, PARP1, PTEN and miR-200a-3p/153-3p/141-3p were investigated by luciferase assay, RNA immunoprecipitation, Western blot and immunohistochemistry.

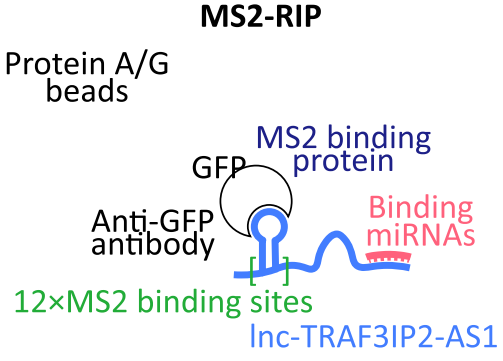
Results: The expression of TRAF3IP2-AS1 was suppressed by NONO-TFE3 fusion in NONO-TFE3 tRCC tissues and cells. Overexpression of TRAF3IP2-AS1 inhibited the proliferation, migration and invasion of UOK109 cells which were derived from cancer tissue of patient with NONO-TFE3 tRCC. Mechanistic studies revealed that TRAF3IP2-AS1 acceler-ated the decay of PARP1 mRNA by direct binding and recruitment of N6-methyladenosie methyltransferase complex. Meanwhile, TRAF3IP2-AS1 competitively bound to miR-200a-3p/153-3p/141-3p and prevented those from decreasing the level of PTEN.

Keywords: TRAF3IP2-AS1, M6A modification, NONO-TFE3, PARP1, PTEN

Journal of Hematology Oncology
2021 Mar 19; 14:46
Impact Factor: 28.5

Materials and Methods

Cy3-labeled TRAF3IP2-AS1 probes were synthesized by **GenePharma** Technology (Shanghai, China). FISH was performed using a **FISH Kit** (**GenePharma**) according to the manufacturer's instructions.



Drug Resistance Updates 68 (2023) 100933

Contents lists available at ScienceDirect

Drug Resistance Updates

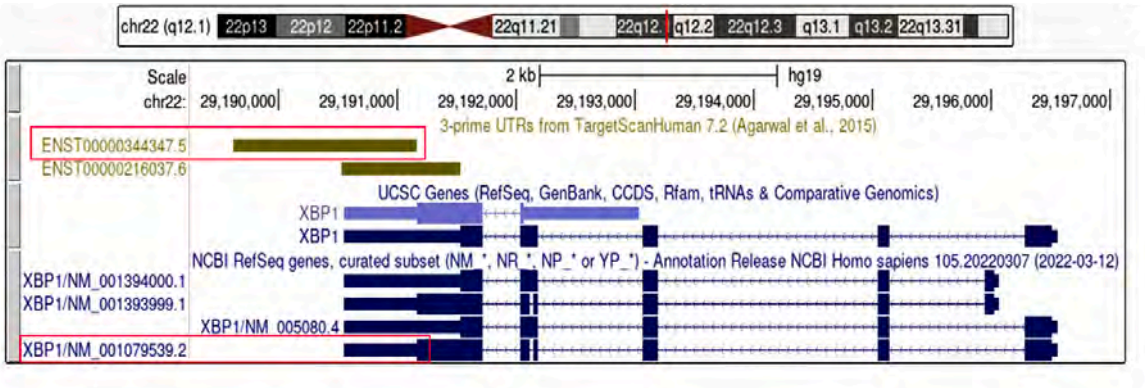
journal homepage: www.elsevier.com/locate/drup

CPSF6-mediated XBP1 3'UTR shortening attenuates cisplatin-induced ER stress and elevates chemo-resistance in lung adenocarcinoma

Chuandong Zhu [a,1], Yufeng Xie [b,1], Qiang Li [c,1], Zhiwei Zhang [b,1], Juan Chen [d], Kai Zhang [d], Xuefeng Xia [e], Danlei Yu [f], Dongqin Chen [g,h,**], Zhengyuan Yu [f,**], Jing Chen [i,*]

A B S T R A C T

Alternative polyadenylation (APA) is a widespread mechanism generating RNA molecules with alternative 3' ends. Herein, we discovered that TargetScan includes a novel XBP1 transcript with a longer 3' untranslated region (UTR) (XBP1-UL) than that included in NCBI. XBP1-UL exhibited a lowered level in blood samples from lung adenocarcinoma (LUAD) patients and in those after DDP treatment. Consistently, XBP1-UL was reduced in A549 cells compared to normal BEAS-2B cells, as well as in DDP-treated/resistant A549 cells relative to controls. Moreover, due to decreased usage of the distal polyadenylation site (PAS) in 3'UTR, XBP1-UL level was lowered in A549 cells and decreased further in DDP-resistant A549 (A549/DDP) cells. Importantly, use of the distal PAS (dPAS) and XBP1-UL level were gradually reduced in A549 cells under increasing concentrations of DDP, which was attributed to DDP-induced endoplasmic reticulum (ER) stress. Furthermore, XBP1 transcripts with shorter 3'UTR (XBP1-US) were more stable and presented stronger potentiation on DDP resistance. The choice of proximal PAS (pPAS) was attributed to CPSF6 elevation, which was caused by BRCA1-distrupted R-loop accu-mulation in CPSF6 5'end. DDP-induced nuclear LINC00221 also facilitated CPSF6-induced pPAS choice in the pre-XBP1 3'end. Finally, we found that unlike the unspliced XBP1 protein (XBP1-u), the spliced form XBP1-s retarded p53 degradation to facilitate DNA damage repair of LUAD cells. The current study provides new in-sights into tumor progression and DDP resistance in LUAD, which may contribute to improved LUAD treatment.



DRUG RESISTANCE UPDATES
2023 Jan 25;68:100933
Impact Factor:24.3

Materials and Methods

Short hairpin RNAs (shRNAs) specifically targeting to XBP1 , CPSF6 , METTL3 , WTAP , BRCA1, LINC00221and p53 were synthesized by Shanghai **GenePharma** (China).
All FISH procedures were in accordance with the manufacturer's instructions of **FISH kit** (**Genepharma**, China).
Briefly,the **biotin-labeled probe** targeting LINC00221 (Bio-LINC00221) was designed and synthesized by **GenePharma**.

nature cell biology

Article

https://doi.org/10.1038/s41556-023-01309-3

A chaperone-like function of FUS ensures TAZ condensate dynamics and transcriptional activation

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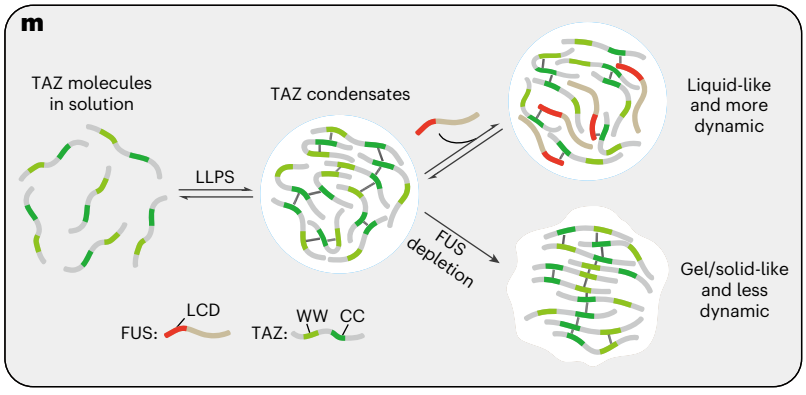
Published online: 3 January 2024

Yangqing Shao[1,8], Xin Shu[1,2,8], Yi Lu[3,8], Wenxuan Zhu[1], Ran Li[4], Huanyi Fu[1], Chengyu Li[1], Wei Sun[1,2], Zhuo Li[1], Yitong Zhang[1], Xiaolei Cao[1], Xifu Ye[3], Emmanuel Ajiboye[5], Bin Zhao[1,2,6,7], Long Zhang[1,2,6], Haifan Wu[5], Xin-Hua Feng[1,2,6,7], Bing Yang[1,2] ✉ & Huasong Lu[1] ✉

The Hippo pathway has important roles in organ development, tissue homeostasis and tumour growth. Its downstream effector TAZ is a transcriptional coactivator that promotes target gene expression through the formation of biomolecular condensates. However, the mechanisms that regulate the biophysical properties of TAZ condensates to enable Hippo signalling are not well understood. Here using chemical crosslinking combined with an unbiased proteomics approach, we show that FUS associates with TAZ condensates and exerts a chaperone-like effect
to maintain their proper liquidity and robust transcriptional activity. Mechanistically, the low complexity sequence domain of FUS targets the coiled-coil domain of TAZ in a phosphorylation-regulated manner, which ensures the liquidity and dynamicity of TAZ condensates. In cells lacking FUS, TAZ condensates transition into gel-like or solid-like assembles with immobilized TAZ, which leads to reduced expression of target genes
and inhibition of pro-tumorigenic activity. Thus, our findings identify a chaperone-like function of FUS in Hippo regulation and demonstrate that appropriate biophysical properties of transcriptional condensates are essential for gene activation.



NATURE CELL BIOLOGY
2024 Jan;26(1):86-99
Impact Factor: 21.3

Materials and Methods

The FISH experiments were conducted per the instructions of a **RNA FISH kit** (**GenePharma**).

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DOI: 10.1002/cac2.70016

CANCER COMMUNICATIONS

ORIGINAL ARTICLE

Blocking ITGA5 potentiates the efficacy of anti-PD-1 therapy on glioblastoma by remodeling tumor-associated macrophages

Rongrong Zhao[1,2] | **Ziwen Pan**[1,2] | **Jiawei Qiu**[1,2] | **Boyan Li**[1,2] | **Yanhua Qi**[1,2] | **Zijie Gao**[1,2] | **Wei Qiu**[1,2] | **Weijie Tang**[1,2] | **Xiaofan Guo**[3] | **Lin Deng**[1,2] | **Gang Li**[1,2] | **Hao Xue**[1,2]

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[2]Shandong Key Laboratory of Brain Health and Function Remodeling, Jinan, P. R. China

[3]Department of Neurology, Loma Linda University Health, Loma Linda, California, USA

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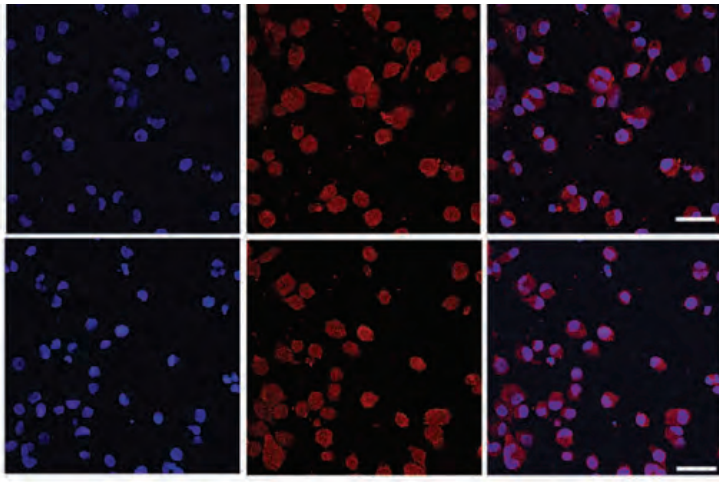
Gang Li, Department of Neurosurgery, Qilu Hospital, Cheeloo College of Medicine and Institute of Brain and Brain-Inspired Science, Shandong University, Jinan 250012, Shandong, P. R. China.
Email: dr.ligang@sdu.edu.cn

Abstract

Background: Glioblastoma (GBM) is largely refractory to antibodies against programmed cell death 1 (anti-PD-1) therapy. Fully understanding the cellular heterogeneity and immune adaptations in response to anti-PD-1 therapy is necessary to design more effective immunotherapies for GBM. This study aimed to dissect the molecular mechanisms of specific immunosuppressive subpopulations to drive anti-PD-1 resistance in GBM.

Methods: We systematically analysed single-cell RNA sequencing and spatial transcriptomics data from GBM tissues receiving anti-PD-1 therapy to characterize the microenvironment alterations. The biological functions of a novel circular RNA (circRNA) were validated both in vitro and in vivo. Mechanically,



Cancer Communications
Accepted: 3 March 2025
Impact Factor: 20.1

Materials and Methods
The **RNA FISH probes** were designed and synthesized by **GenePharma** (Shanghai, China).

ADVANCED FUNCTIONAL MATERIALS
www.afm-journal.de

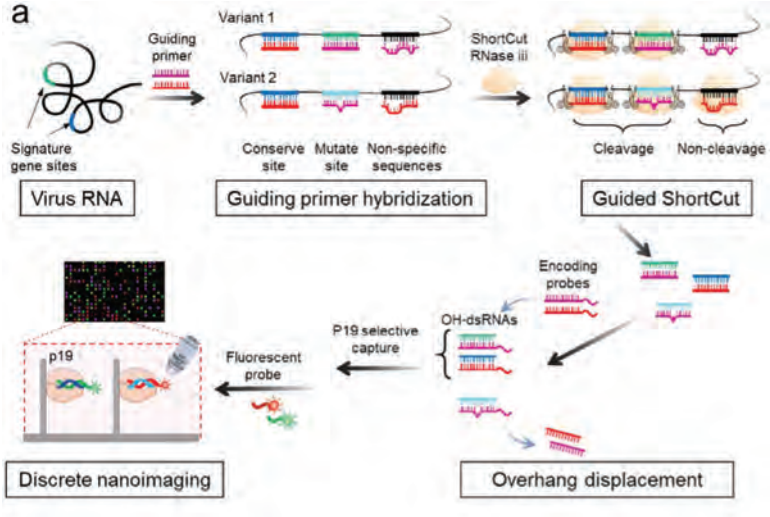
Amplification-Free, Sequencing-Free, Detection of Viral RNAs with Variant Specification by Discrete Nanocounting

Zixun Wang, Xi Zhao, Wan-Mui Chan, Xianglin Ji, Linfeng Huang, Xi Xie, Wei Li, Wenjun Zhang, Kelvin Kai-Wang To, and Peng Shi**

This study describes an amplification-free, sequencing-free platform (NanoPick-array) for fast analysis of viral RNAs. The platform combines selective short-cut of viral RNAs, cherry-picking isolation of target genes, and micro-arrayed discrete nanoimaging to enable the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at a concentration of 60 copies μL^{-1}, a detection limit that is hardly achieved by Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-based methods without amplification, regardless of electrochemical or colorimetric approaches. Notably, the NanoPick-array provides specific virus variant information with differentiation to single-nucleotide genetic mutation. The avoidance of the amplification procedure gives direct quantification of viral copy number and reduces false positive results caused by amplicon contamination; the sequencing-free viral variant specification significantly reduces the turn-over time for the acquisition of a complete diagnostic viral picture within just 2 h. In a demonstration using clinical samples with a wide range of viral loads of cycle threshold (Ct) value ranging from 18 to 36, the technique achieves an overall accuracy of 89.7% viral detection and 100% accuracy for identifying all Delta variants. The viral detection accuracy is further tested to be 100% for the clinical samples with Ct values around or less than 28.

1. Introduction

In past few decades, significant risk of infectious epidemic has been attributed to the pathogenic single-stranded RNA virus, such as severe acute respiratory syndrome coronavirus (SARS-CoV), middle east respiratory syndrome coronavirus (MERS-CoV), human immunodeficiency virus (HIV), Zika virus and Ebola virus. Particularly, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, started in late 2019, haunted for over 3 years, and caused significant damage to both public health and social stability worldwide. One of the reasons for the rapid and continuous spreading of SARS-CoV-2 is the prevalence of presymptomatic and asymptomatic transmission,[1] which is getting worse in silent transmission as the virus undergoes fast genetic mutation, from the initial Alpha virus lineage (B.1.1.7) to the later Omicron variant (B.1.1.529). In many cases, different SARS-CoV-2 variants differ by only one



ADVANCED FUNCTIONAL MATERIALS
2024 Feb 20;2310157
Impact Factor: 19

Materials and Methods

The **RNA probes** (Guiding primers and overhang En-coding probes) were synthesized from **GenePharma**.

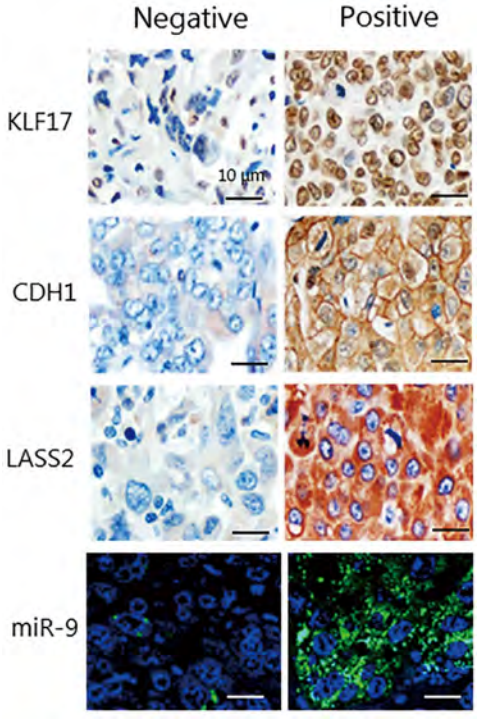
SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Derepression of co-silenced tumor suppressor genes by nanoparticle-loaded circular ssDNA reduces tumor malignancy

Jing Meng,[1]* Shuang Chen,[2]* Jing-xia Han,[1] Qiang Tan,[1] Xiao-rui Wang,[3] Hong-zhi Wang,[1,2] Wei-long Zhong,[1] Yuan Qin,[1] Kai-liang Qiao,[1,2] Chao Zhang,[1,2] Wan-feng Gao,[1,2] Yue-yang Lei,[1,2] Hui-juan Liu,[2,3] Yan-rong Liu,[2] Hong-gang Zhou,[1] Tao Sun,[1,2†] Cheng Yang[1,2†]

The co-silencing of multiple tumor suppressor genes can lead to escalated malignancy in cancer cells. Given the limited efficacy of anticancer therapies targeting single tumor suppressor genes, we developed small circular single-stranded DNA (CSSD) that can up-regulate the expression of co-silenced tumor suppressor genes by sequestering microRNAs (miRNAs) that negatively regulate these genes. We found that cancer patients with low tumor expression of the tumor suppressor genes KLF17, CDH1, and LASS2 had shortened survival times. The up-regulation of these genes upon transfection of artificial CSSD-9 inhibited tumor proliferation and metastasis and promoted apoptosis in vitro as well as in ex vivo and patient-derived xenograft models. In addition, CSSD is more stable and effective than current miRNA inhibitors, and transfecting CSSDs via nanoparticles substantially improved delivery efficiency. The use of a single CSSD can promote the inhibition of multiple tumor suppressor genes. This study provides evidence for the possibility of using CSSDs as therapeutic miRNA inhibitors to target the co-silencing of multiple tumor suppressor genes.



Science Translational Medicine
2018 May 23;10(442):eaao6321
Impact Factor: 17.1

Materials and Methods

Fluorescence in situ hybridization **FAM-labeled locked nucleic acid-modified oligonucleotide probes** complementary to mature miR-9 were purchased from **GenePharma**.

nature communications

Article

https://doi.org/10.1038/s41467-023-43974-w

LncRNA MIR200CHG inhibits EMT in gastric cancer by stabilizing miR-200c from target-directed miRNA degradation

Received: 27 January 2023

Accepted: 26 November 2023

Published online: 08 December 2023

Yixiao Zhu[1,2,3,6], Chengmei Huang[1,6], Chao Zhang[1,6], Yi Zhou[1,6], Enen Zhao[1], Yaxin Zhang[1], Xingyan Pan[1], Huilin Huang[1] ✉, Wenting Liao[1] ✉ & Xin Wang[2,4,5] ✉

Gastric cancer (GC) is a heterogeneous disease, threatening millions of lives worldwide, yet the functional roles of long non-coding RNAs (lncRNAs) in different GC subtypes remain poorly characterized. Microsatellite stable (MSS)/epithelial-mesenchymal transition (EMT) GC is the most aggressive subtype associated with a poor prognosis. Here, we apply integrated network analysis to uncover lncRNA heterogeneity between GC subtypes, and identify MIR200CHG as a master regulator mediating EMT specifically in MSS/EMT GC. The expression of MIR200CHG is silenced in MSS/EMT GC by promoter hypermethylation, associated with poor prognosis. MIR200CHG reverses the mesenchymal identity of GC cells in vitro and inhibits metastasis in vivo. Mechanistically, MIR200CHG not only facilitates the biogenesis of its intronic miRNAs miR-200c and miR-141, but also protects miR-200c from target-directed miRNA degradation (TDMD) through direct binding to miR-200c. Our studies reveal a landscape of a subtype-specific lncRNA regulatory network, providing clinically relevant biological insights towards MSS/EMT GC.

Nature Communications
2023 Dec 8;14(1):8141
Impact Factor: 16.6

Materials and Methods

Subcellular localization of MIR200CHG was detected using the **cellular RNA FISH Kit** (**GenePharma**, Shanghai, China).
Cy3-labeled MIR200CHG probes were obtained from **GenePharma** (Shanghai, China).

nature communications

Article

https://doi.org/10.1038/s41467-023-40212-1

Circular RNA encoded MET variant promotes glioblastoma tumorigenesis

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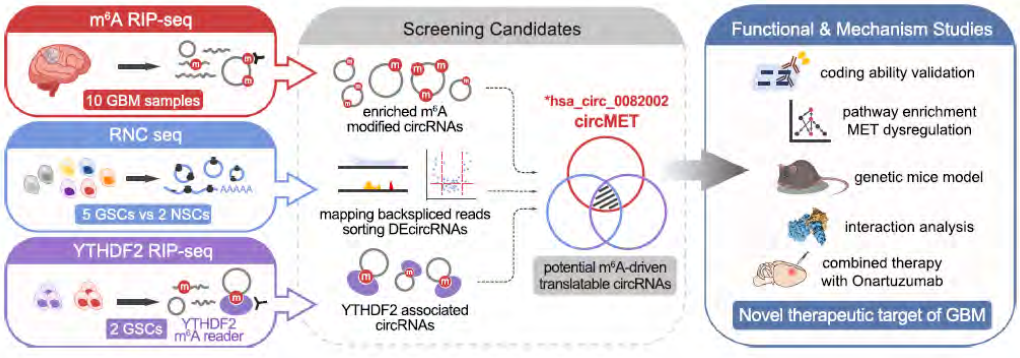
Jian Zhong[1,2,12], Xujia Wu[1,2,12], Yixin Gao[1,2,12], Junju Chen[1,2,12], Maolei Zhang[1,2], Huangkai Zhou[1,2], Jia Yang[1,2], Feizhe Xiao[3], Xuesong Yang[1,2], Nunu Huang[1,2], Haoyue Qi[4,5], Xiuxing Wang[6,7,8,9] ✉, Fan Bai[10,11] ✉, Yu Shi[4,5] ✉ & Nu Zhang[1,2] ✉

Activated by its single ligand, hepatocyte growth factor (HGF), the receptor tyrosine kinase MET is pivotal in promoting glioblastoma (GBM) stem cell self-renewal, invasiveness and tumorigenicity. Nevertheless, HGF/MET-targeted therapy has shown limited clinical benefits in GBM patients, suggesting hidden mechanisms of MET signalling in GBM. Here, we show that circular MET RNA (circMET) encodes a 404-amino-acid MET variant (MET404) facilitated by the N^6-methyladenosine (m^{6}A) reader YTHDF2. Genetic ablation of circMET inhi-bits MET404 expression in mice and attenuates MET signalling. Conversely, MET404 knock-in (KI) plus *P53* knock-out (KO) in mouse astrocytes initiates GBM tumorigenesis and shortens the overall survival. MET404 directly inter-acts with the MET β subunit and forms a constitutively activated MET receptor whose activity does not require HGF stimulation. High MET404 expression predicts poor prognosis in GBM patients, indicating its clinical relevance. Targeting MET404 through a neutralizing antibody or genetic ablation redu-ces GBM tumorigenicity in vitro and in vivo, and combinatorial benefits are obtained with the addition of a traditional MET inhibitor. Overall, we identify a MET variant that promotes GBM tumorigenicity, offering a potential ther-apeutic strategy for GBM patients, especially those with MET hyperactivation.



Nature Communications
2023 Jul;14:4467
Impact Factor: 16.6

Materials and Methods

GSCs were infected with the above lentiviruses using **polybrene** (8 μg/ml, **GenePharma**) for up to 48 h. FISH assays were performed using an **RNA FISH kit** (**GenePharma**, China) according to the manufacturer's instructions.

All the **siRNAs** and **shRNAs** used in this study were generated by **GenePharma**.

nature communications

Article

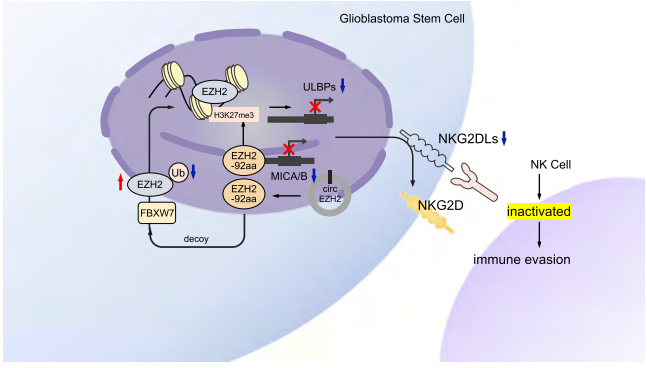
https://doi.org/10.1038/s41467-022-32311-2

Circular EZH2-encoded EZH2-92aa mediates immune evasion in glioblastoma via inhibition of surface NKG2D ligands

Glioblastoma (GBM) is a highly aggressive primary brain tumour and is resis-tant to nearly all available treatments, including natural killer (NK) cell immunotherapy. However, the factors mediating NK cell evasion in GBM remain largely unclear. Here, we report that EZH2-92aa, a protein encoded by circular EZH2, is overexpressed in GBM and induces the immune evasion of GBM stem cells (GSCs) from NK cells. Positively regulated by DEAD-box heli-case 3 (DDX3), EZH2-92aa directly binds the major histocompatibility complex class I polypeptide-related sequence A/B (MICA/B) promoters and represses their transcription; it also indirectly represses UL16-binding protein (ULBP) transcription by stabilizing EZH2. The downregulation of NK group 2D ligands (NKG2DLs, including MICA/B and ULBPs) in GSCs mediates NK cell resistance. Moreover, stable EZH2-92aa knockdown enhances NK cell-mediated GSC eradication in vitro and in vivo and synergizes with anti-PD1 therapy. Our results highlight the immunosuppressive function of EZH2-92aa in inhibiting theNKcellresponseinGBMandtheclinical potential of targeting EZH2-92aa for NK-cell-directed immune therapy.

Glioblastoma (GBM) is the most lethal primary brain tumour in adults. Despite aggressive treatments, including surgical resection, radio-therapy and chemotherapy, the outcomes of patients with GBM are dismal, with a median survival time of <2 years and a 5-year survival rate of only 5.8%1. While recent advances in cancer immunotherapy have improved patient outcomes in certain types of cancer, the immunosuppressive tumour microenvironment (TME) of GBM poses a major therapeutic challenge in malignant brain cancers2,3.

Natural killer (NK) cells are large granular lymphocytes that can spontaneously lyse malignant cells, including GBM stem cells (GSCs)4–6, suggesting their distinct advantages over T cells for therapeutic approaches7–9. However, the results of clinical trials using NK cells to target GBM were largely unsatisfactory10, prompting studies on the mechanism by which GSCs evade NK cell surveillance and eradication. NK cell cytotoxicity is facilitated by an array of activating receptors11. Disruption of receptor–ligand inter-actions between NK cells and GSCs is the primary determinant of NK cell resistance, as downregulation of NK group 2D (NKG2D) ligands is frequently observed in GBM12,13. However, the factors that deter-mine the aberrant expression of NKG2D ligands remain largely unknown.



Nature Communications
2022 Aug;13(1):1-18
Impact Factor: 16.6

Materials and Methods

Cy3-labelled oligonucleotide probes complementary to the circEZH2 junction sequence were synthesized by **GenePharma** (Jiangsu, China).

SiRNAs were obtained from **GenePharma** (Jiangsu, China).

Lentiviral shRNA vectors were obtained from **GenePharma** (Jiangsu, China).

To establish stable cell lines, GSCs were transduced with the above lentiviral vectors in culture medium containing 8 μg/ml **polybrene** (**GenePharma**).

ADVANCED SCIENCE Open Access
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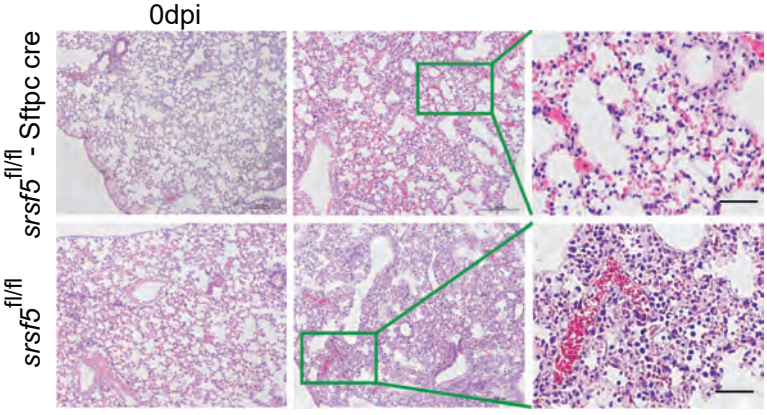
SRSF5-Mediated Alternative Splicing of M Gene is Essential for Influenza A Virus Replication: A Host-Directed Target Against Influenza Virus

Qiuchen Li, Zhimin Jiang, Shuning Ren, Hui Guo, Zhimin Song, Saini Chen, Xintao Gao, Fanfeng Meng, Junda Zhu, Litao Liu, Qi Tong, Honglei Sun, Yipeng Sun, Juan Pu, Kin-Chow Chang, and Jinhua Liu**

Splicing of influenza A virus (IAV) RNA is an essential process in the viral life cycle that involves the co-opting of host factors. Here, it is demonstrated that induction of host serine and arginine-rich splicing factor 5 (SRSF5) by IAV facilitated viral replication by enhancing viral M mRNA splicing. Mechanistically, SRSF5 with its RRM2 domain directly bounds M mRNA at conserved sites (M mRNA position 163, 709, and 712), and interacts with U1 small nuclear ribonucleoprotein (snRNP) to promote M mRNA splicing and M2 production. Mutations introduced to the three binding sites, without changing amino acid code, significantly attenuates virus replication and pathogenesis in vivo. Likewise, SRSF5 conditional knockout in the lung protects mice against lethal IAV challenge. Furthermore, anidulafungin, an approved antifungal drug, is identified as an inhibitor of SRSF5 that effectively blocks IAV replication in vitro and in vivo. In conclusion, SRSF5 as an activator of M mRNA splicing promotes IAV replication and is a host-derived antiviral target.

Influenza A viruses (IAVs) are prevalent in many mammalian and avian host species, and periodically cause epidemics or pan-demics in humans, and epizootics or panzootics in animals.Globally each year, there are around one bil-lion human infections of which 3–5 mil-lion are clinically critical with 300 000–600 000 ensuing deaths (https://www.cdc. gov/flu/season/index.html). Presently, with the ongoing COVID-19 pandemic, there are concerns of reduced population immunity against influenza viruses from prolonged shielding and reduced exposure. Annual in-fluenza vaccination is still the most effective protection available against the highly mu-table virus. All antivirals that target specific influenza viral components (such as M2 ion channel, neuraminidase, and polymerase subunit PA) are known to readily cause virus resistance which greatly limits their usefulness. Rather than directly target-ing viral components, it has been suggested that a cell-based approach that targets key host-dependent factor(s) necessary for viral replication could confer reduced virus resistance and broad-spectrum efficacy. Recently, it was found that thapsigargin, a sarco-endoplasmic Ca2+-ATPase pump inhibitor, is a highly po-tent broad-spectrum host-centric antiviral against three major human respiratory viruses: influenza A virus, SARS-CoV-2, and respiratory syncytial virus.



Advanced Science
2022 Oct;:2203088
Impact Factor: 15.1

Materials and Methods

Cells were then hybridized with Alexa Fluor 488-conjugated **M RNA target probes** (M-probes, **GenePharma**) of PR8 virus in hybridization buffer for 10 min at 75 °C.

ADVANCED SCIENCE Open Access
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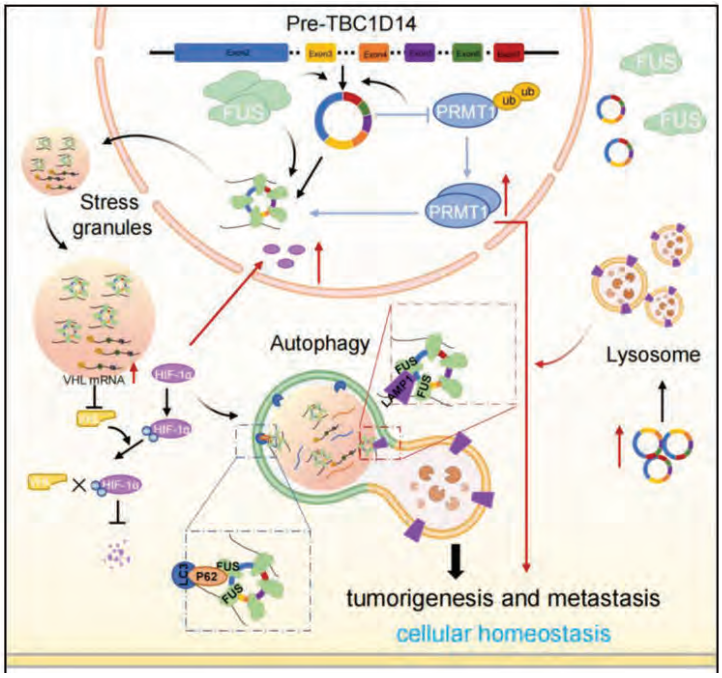
Hypoxia-Induced FUS–circTBC1D14 Stress Granules Promote Autophagy in TNBC

*Ying Liu, Yiwei Liu, Yinqiao He, Ning Zhang, Siyue Zhang, Yaming Li, Xiaolong Wang, Yiran Liang, Xi Chen, Weijing Zhao, Bing Chen, Lijuan Wang, Dan Luo, and Qifeng Yang**

Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer that is suggested to be associated with hypoxia. This study is the first to identify a novel circular RNA (circRNA), circTBC1D14, whose expression is significantly upregulated in TNBC. The authors confirm that high circTBC1D14 expression is associated with a poor prognosis in patients with breast cancer. circTBC1D14-associated mass spectrometry and RNA-binding protein-related bioinformatics strategies indicate that FUS can interact with circTBC1D14, which can bind to the downstream flanking sequence of circTBC1D14 to induce cyclization. FUS is an essential biomarker associated with stress granules (SGs), and the authors find that hypoxic conditions can induce FUS–circTBC1D14-associated SG formation in the cytoplasm after modification by protein PRMT1. Subsequently, circTBC1D14 increases the stability of PRMT1 by inhibiting its K48-regulated polyubiquitination, leading to the upregulation of PRMT1 expression. In addition, FUS–circTBC1D14 SGs can initiate a cascade of SG-linked proteins to recognize and control the elimination of SGs by recruiting LAMP1 and enhancing lysosome-associated autophagy flux, thus contributing to the maintenance of cellular homeostasis and promoting tumor progression in TNBC. Overall, these findings reveal that circTBC1D14 is a potential prognostic indicator that can serve as a therapeutic target for TNBC treatment.



Advanced Science
2023 Feb 19;2204988
Impact Factor: 15.1

Materials and Methods

RNA FISH assay was executed using a **specific probe** synthesized by **Genepharma** company. The prehybridization and hybridization experiments were carried out by the **Fluorescent in Situ Hybridization Kit** (**Genepharma**).
Lipofectamine 2000 was used in the study to help individual **siRNAs** (**GenePharma**) transfect into cells.

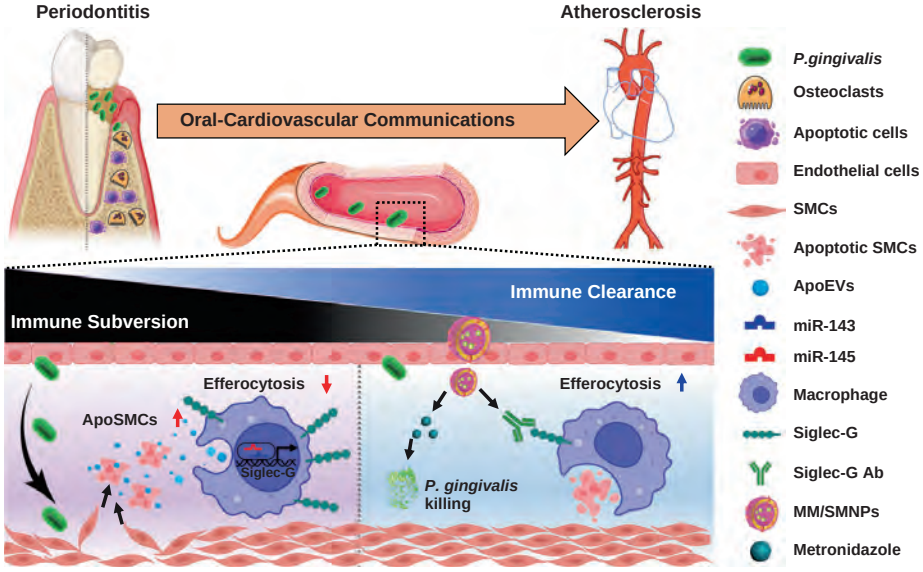
ARTICLE OPEN

Oral pathogen aggravates atherosclerosis by inducing smooth muscle cell apoptosis and repressing macrophage efferocytosis

Hanyu Xie[1,2,3], Ziyue Qin[2,3,4], Ziji Ling[1,2,3], Xiao Ge[1,2,3], Hang Zhang[1,2,3], Shuyu Guo[2,3,5], Laikui Liu[2,3], Kai Zheng[2,3], Hongbing Jiang[1,2,3]✉ and Rongyao Xu[1,2,3]✉

Periodontitis imparting the increased risk of atherosclerotic cardiovascular diseases is partially due to the immune subversion of the oral pathogen, particularly the *Porphyromonas gingivalis* (*P. gingivalis*), by inducing apoptosis. However, it remains obscure whether accumulated apoptotic cells in *P. gingivalis*-accelerated plaque formation are associated with impaired macrophage clearance. Here, we show that smooth muscle cells (SMCs) have a greater susceptibility to *P. gingivalis*-induced apoptosis than endothelial cells through TLR2 pathway activation. Meanwhile, large amounts of miR-143/145 in *P.gingivalis*-infected SMCs are extracellularly released and captured by macrophages. Then, these miR-143/145 are translocated into the nucleus to promote Siglec-G transcription, which represses macrophage efferocytosis. By constructing three genetic mouse models, we further confirm the in vivo roles of TLR2 and miR-143/145 in *P. gingivalis*-accelerated atherosclerosis. Therapeutically, we develop *P.gingivalis*-pretreated macrophage membranes to coat metronidazole and anti-Siglec-G antibodies for treating atherosclerosis and periodontitis simultaneously. Our findings extend the knowledge of the mechanism and therapeutic strategy in oral pathogen-associated systemic diseases.

International Journal of Oral Science (2023)15:26 ; https://doi.org/10.1038/s41368-023-00232-5



International Journal of Oral Science
2023 Jun 28;15:26
Impact Factor: 14.9

Materials and Methods

FISH probes were directly labeled with **Fluorescent In Situ Hybridization Kit** (**Genepharma**, Shanghai, China) according to the manufacturer's instructions, and the **probes** were designed and synthesized by **Genepharma**.
miRNA mimics and **inhibitors** were synthesized and purchased by **GenePharma**.

nature chemical biology

Article

https://doi.org/10.1038/s41589-023-01384-5

Gelation of cytoplasmic expanded CAG RNA repeats suppresses global protein synthesis

Received: 30 January 2023

Accepted: 13 June 2023

Published online: 17 August 2023

Check for updates

Yuyin Pan[1,4], Junmei Lu[1,4], Xinran Feng[1,4], Shengyi Lu[1,4], Yi Yang[2], Guang Yang[1], Shudan Tan[1], Liang Wang[3], Pilong Li[3], Shouqing Luo[2] ✉ & Boxun Lu[1] ✉

RNA molecules with the expanded CAG repeat (eCAGr) may undergo sol–gel phase transitions, but the functional impact of RNA gelation is completely unknown. Here, we demonstrate that the eCAGr RNA may form cytoplasmic gel-like foci that are rapidly degraded by lysosomes. These RNA foci may significantly reduce the global protein synthesis rate, possibly by sequestering the translation elongation factor eEF2. Disrupting the eCAGr RNA gelation restored the global protein synthesis rate, whereas enhanced gelation exacerbated this phenotype. eEF2 puncta were significantly enhanced in brain slices from a knock-in mouse model and from patients with Huntington's disease, which is a CAG expansion disorder expressing eCAGr RNA. Finally, neuronal expression of the eCAGr RNA by adeno-associated virus injection caused significant behavioral deficits in mice. Our study demonstrates the existence of RNA gelation inside the cells and reveals its functional impact, providing insights into repeat expansion diseases and functional impacts of RNA phase transition.

AutophagyNature Chemical Biology
2023 Aug 17;19(11):1372-1383
Impact Factor: 14.8

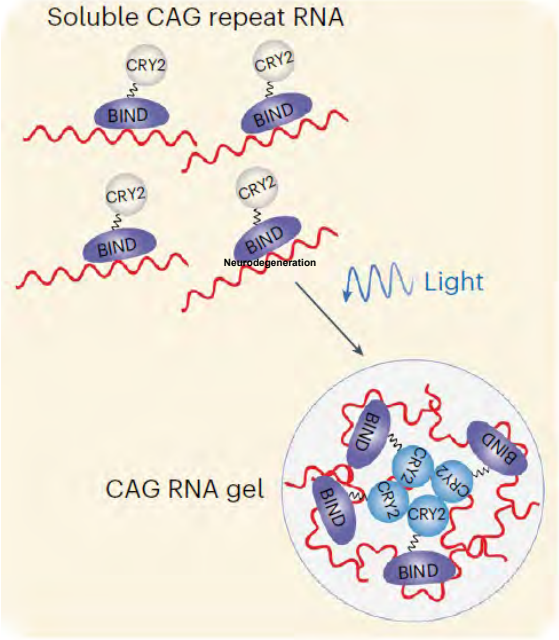
Materials and Methods

RNA FISH was determined using an **RNA FISH kit** from **GenePharma** Technologies per the manufacturer's instructions.

The slice was incubated with an RNA probe designed against the **HTT sequence** (synthesized by **GenePharma** Technologies).

RNA was probed by Cy3-labeled DNA oligonucleotides designed against the **CAG sequence** (synthesized by **GenePharma** Technologies).

Hybridization and **wash buffers** were purchased from **GenePharma** Technologies and used according to the manufacturer's protocols.



Biomaterials 291 (2022) 121869

Contents lists available at ScienceDirect

Biomaterials

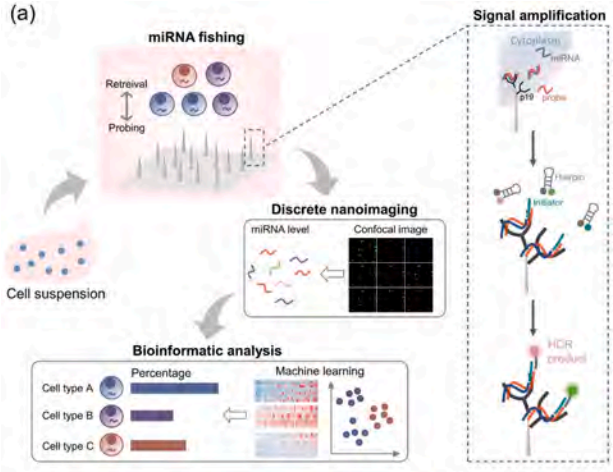
journal homepage: www.elsevier.com/locate/biomaterials

Discrete single-cell microRNA analysis for phenotyping the heterogeneity of acute myeloid leukemia

Xi Zhao [a,d], Zixun Wang [a,f], Xianglin Ji [a,d], Shuyu Bu [b], Peilin Fang [a], Yuan Wang [a], Mingxue Wang [a], Yang Yang [g], Wenjun Zhang [b,e,**], Anskar Y.H. Leung [c,***], Peng Shi [a,d,e,h,*]

Abstract

Acute myeloid leukemia (AML) is a highly heterogenous cancer in hematopoiesis, and its subtype specification is greatly important in the clinical practice for AML diagnosis and prognosis. Increasing evidence has shown the association between microRNA (miRNA) phenotype and AML therapeutic outcomes, emphasizing the need for novel techniques for convenient, sensitive, and efficient miRNA profiling in clinical practices. Here, we describe a nanoneedle-based discrete single-cell microRNA profiling technique for multiplexed phenotyping of AML heterogeneity without the requirement of sequencing or polymerase chain reaction (PCR). In virtue of a biochip- based and non-destructive nature of the assay, the expression of nine miRNAs in large number of living AML cells can be simultaneously analyzed with discrete single-cell level information, thus providing a proof-of- concept demonstration of an AML subtype classifier based on the multidimensional miRNA data. We showed successful analysis of subtype-specific cellular composition with over 90% accuracy and identified drug- responsive leukemia subpopulations among a mixed suspension of cells modeling different AML subtypes. The adoption of machine learning algorithms for processing the large-scale nanoneedle-based miRNA data shows the potential for powerful prediction capability in clinical applications to assist therapeutic decisions. We believe that this platform provides an efficient and cost-effective solution to move forward the translational prognostic usage of miRNAs in AML treatment and can be readily and advantageously applied in analyzing rare patient- derived clinical samples.



BIOMATERIALS
2022 Dec;291:121869
Impact Factor: 14

Materials and Methods

Single-stranded RNA probes complementary to miRNA targets were predesigned and synthesized by **GenePharma** (Shanghai).

AUTOPHAGY
https://doi.org/10.1080/15548627.2023.2196889

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Check for updates

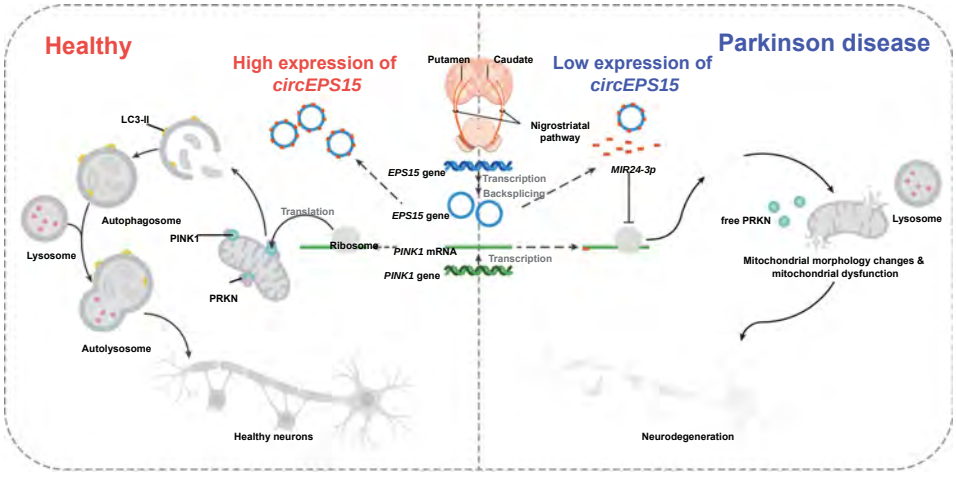
CircEPS15, as a sponge of *MIR24-3p* ameliorates neuronal damage in Parkinson disease through boosting PINK1-PRKN-mediated mitophagy

Yuanzhang Zhou[a*], Yang Liu[b*], Zhengwei Kang[a], Hang Yao[a], Nanshan Song[a], Min Wang[c], Chenghuan Song[a], Kezhong Zhang[d], Jianhua Ding[a], Juanjuan Tang[b], Gang Hu[a,b], and Ming Lu[a]

ABSTRACT

Despite growing evidence that has declared the importance of circRNAs in neurodegenerative diseases, the clinical significance of circRNAs in dopaminergic (DA) neuronal degeneration in the pathogenesis of Parkinson disease (PD) remains unclear. Here, we performed rRNA-depleted RNA sequencing and detected more than 10,000 circRNAs in the plasma samples of PD patients. In consideration of ROC and the correlation between Hohen-Yahr stage (H-Y stage) and Unified Parkinson Disease Rating Scale-motor score (UPDRS) of 40 PD patients, *circEPS15* was selected for further research. Low expression of *circEPS15* was found in PD patients and there was a negative positive correlation between the *circEPS15* level and severity of PD motor symptoms, while over-expression of *circEPS15* protected DA neurons against neurotoxin-induced PD-like neurodegenera-tion *in vitro* and *in vivo*. Mechanistically, *circEPS15* acted as a *MIR24-3p* sponge to promote the stable expression of target gene *PINK1*, thus enhancing PINK1-PRKN-dependent mitophagy to eliminate damaged mitochondria and maintain mitochondrial homeostasis. Thus, *circEPS15* rescued DA neu-ronal degeneration through the *MIR24-3p*-PINK1 axis-mediated improvement of mitochondrial func-tion. This study reveals that *circEPS15* exerts a critical role in participating in PD pathogenesis, and may give us an insight into the novel avenue to develop potential biomarkers and therapeutic targets for PD.

Abbreviations: AAV: adeno-associated virus; DA: dopaminergic; FISH: fluorescence in situ hybridiza-tions; HPLC: high-performance liquid chromatography; H-Y stage: Hohen-Yahr stage; LDH: lactate dehydrogenase; MMP: mitochondrial membrane potential; MPTP/p: 1-methyl-4-phenyl-1,2,3,6-tetra-hydropyridine/probenecid; NC: negative control; PD: Parkinson disease; PINK1: PTEN induced kinase 1; PBS: phosphate-buffered saline; ROS: reactive oxygen species; SNpc: substantia nigra pars com-pacta; TEM: transmission electron microscopy; UPDRS: Unified Parkinson's Disease Rating Scale-motor score



Autophagy
2023 Apr 10 ;2520-2537
Impact Factor: 13.3

Materials and Methods

GenePharma designed and produced FAM-labeled MIR24-3p and Cy3-labeled circEPS15 probes. The fluorescent in Situ Hybridization Kit (GenePharma, China) was used to detect the probes, and images were obtained using confocal scanning laser microscope (Carl Zeiss).

The MIR24-3p and PINK1 siRNA (GenePharma, GY20200928RFF) were transfected at a concentration of 50 nM.

KSBMB
Korean Society for Biochemistry and Molecular Biology

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ARTICLE OPEN

Check for updates

LncRNA KIAA0087 suppresses the progression of osteosarcoma by mediating the SOCS1/JAK2/STAT3 signaling pathway

Haoli Gong[1], Ye Tao[2], Sheng Xiao[1], Xin Li[1], Ke Fang[1], Jie Wen[1], Pan He[1] and Ming Zeng[1]✉

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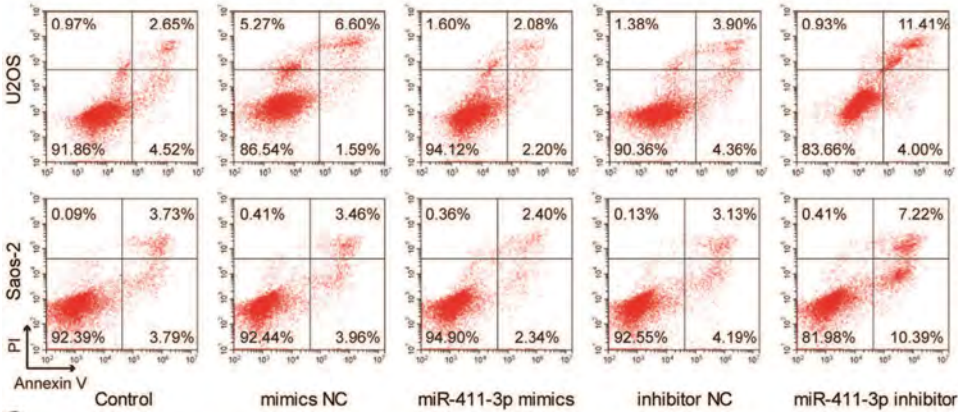
Long noncoding RNAs (lncRNAs), widely expressed in mammalian cells, play pivotal roles in osteosarcoma (OS) progression. Nevertheless, the detailed molecular mechanisms of lncRNA KIAA0087 in OS remain obscure. Here, the roles of KIAA0087 in OS tumorigenesis were investigated. KIAA0087 and miR-411-3p levels were detected by RT-qPCR. Malignant properties were assessed by CCK-8, colony formation, flow cytometry, wound healing, and transwell assays. SOCS1, EMT, and JAK2/STAT3 pathway-related protein levels were measured by western blotting. Direct binding between miR-411-3p and KIAA0087/SOCS1 was validated by a dual-luciferase reporter, RIP, and FISH assays. In vivo growth and lung metastasis were evaluated in nude mice. The expression levels of SOCS1, Ki-67, E-cadherin, and N-cadherin in tumor tissues were measured by immunohistochemical staining. Downregulation of KIAA0087 and SOCS1 and upregulation of miR-411-3p were found in OS tissues and cells. Low expression of KIAA0087 was associated with a poor survival rate. Forced expression of KIAA0087 or miR-411-3p inhibition repressed the growth, migration, invasion, EMT, and activation of the JAK2/STAT3 pathway and triggered apoptosis of OS cells. However, the opposite results were found with KIAA0087 knockdown or miR-411-3p overexpression. Mechanistic experiments indicated that KIAA0087 enhanced SOCS1 expression to inactivate the JAK2/STAT3 pathway by sponging miR-411-3p. Rescue experiments revealed that the antitumor effects of KIAA0087 overexpression or miR-411-3p suppression were counteracted by miR-411-3p mimics or SOCS1 inhibition, respectively. Finally, in vivo tumor growth and lung metastasis were inhibited in KIAA0087-overexpressing or miR-411-3p-inhibited OS cells. In summary, the downregulation of KIAA0087 promotes the growth, metastasis, and EMT of OS by targeting the miR-411-3p-mediated SOCS1/JAK2/STAT3 pathway.

Experimental & Molecular Medicine (2023) 55:831–843; https://doi.org/10.1038/s12276-023-00972-8



EXPERIMENTAL AND MOLECULAR MEDICINE
2023 Apr 10 ;55:831–843
Impact Factor: 12.8

Materials and Methods

Cy3-labeled KIAA0087 and FITC-labeled miR-411-3p probes were pur-chased from **GenePharma**. The probe signals were determined with **a FISH Probe Kit** from **GenePharma**.

CDD press

www.nature.com/cdd

ARTICLE OPEN

Check for updates

LncRNA NEAT1 controls the lineage fates of BMSCs during skeletal aging by impairing mitochondrial function and pluripotency maintenance

Hengguo Zhang[1,2,6], Rongyao Xu[1,2,6], Bang Li[1,2], Zhili Xin[1,2], Ziji Ling[1,2], Weiwen Zhu[1,2], Xiang Li[1,2], Ping Zhang[1,2], Yu Fu[1,2], Jiyu Chen[3], Laikui Liu[1,4], Jie Cheng[1,2] and Hongbing Jiang[1,2,5]✉

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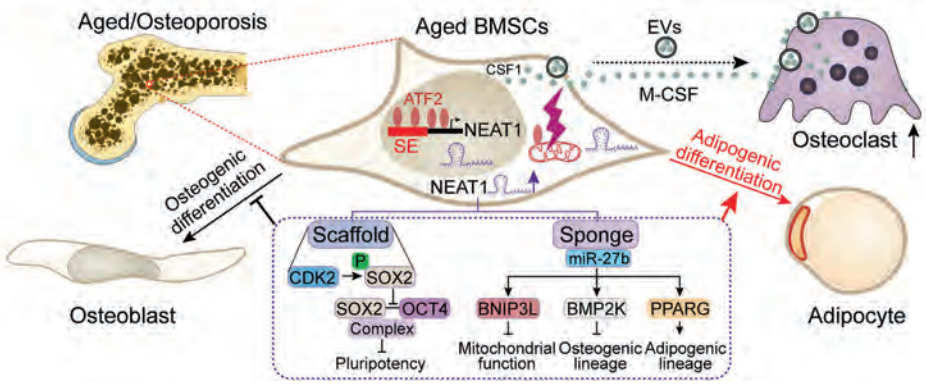
Aged bone marrow mesenchymal stem cells (BMSCs) exhibit aberrant self-renewal and lineage specification, which contribute to imbalanced bone-fat and progressive bone loss. In addition to known master regulators of lineage commitment, it is crucial to identify pivotal switches governing the specific differentiation fate of aged BMSCs. Here, we profiled differences in epigenetic regulation between adipogenesis and osteogenesis and identified super-enhancer associated lncRNA nuclear-enriched abundant transcript 1 (NEAT1) as a key bone-fat switch in aged BMSCs. We validated that NEAT1 with high enhancer activity was transcriptionally activated by ATF2 and directed aged BMSCs to a greater propensity to differentiate toward adipocytes than osteoblasts by mediating mitochondrial function. Furthermore, we confirmed NEAT1 as a protein-binding scaffold in which phosphorylation modification of SOX2 Ser249/250 by CDK2 impaired SOX2/OCT4 complex stability and dysregulated downstream transcription networks of pluripotency maintenance. In addition, by sponging miR-27b-3p, NEAT1 upregulated BNIP3L, BMP2K, and PPARG expression to shape mitochondrial function and osteogenic/adipogenic differentiation commitment, respectively. In extracellular communication, NEAT1 promoted CSF1 secretion from aged BMSCs and then strengthened osteoclastic differentiation by extracellular vesicle delivery. Notably, Neat1 small interfering RNA delivery induced increased bone mass in aged mice and decreased fat accumulation in the bone marrow. These findings suggest that NEAT1 regulates the lineage fates of BMSCs by orchestrating mitochondrial function and pluripotency maintenance, and might be a potential therapeutic target for skeletal aging.



Cell Death & Differentiation
2021 Sep 8;29(2):351-365
Impact Factor: 12.4

Materials and Methods

5′Biotin-labeled oligonucleotide probes targeting the junction sites of sense and antisense NEAT1 (NR_028272) were designed and synthesized (**GenePharma**, Shanghai, China). The miRNA pulldown assay was performed using **biotinylated miR-27b-3p mimic** and **miR-27b-3p mimic NC** (**GenePharma**, Shanghai, China).

IVYSPRING INTERNATIONAL PUBLISHER

Theranostics

Research Paper

2021; 11(19): 9623-9651. doi: 10.7150/thno.64880

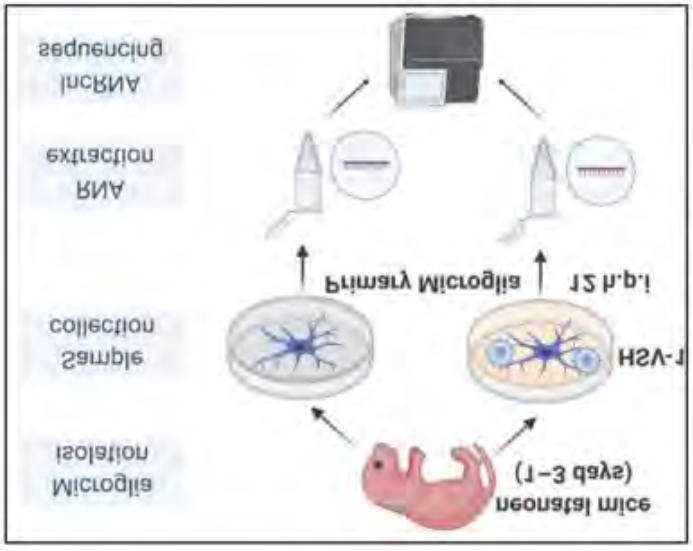
A novel lncRNA linc-AhRA negatively regulates innate antiviral response in murine microglia upon neurotropic herpesvirus infection

Yiliang Wang[1,2,3,4], Weisheng Luo[1,2,3,4], Lianzhou Huang[1,2,3,4], Ji Xiao[1,2,3,4], Xiaowei Song[1,2,3,4], Feng Li[1,2,3,4], Yuying Ma[1,2,3,4], Xiaohui Wang[1,2,3,4], Fujun Jin[1,2,3,4], Ping Liu[1,2,3,4], Yexuan Zhu[1,2,3,4], Kaio Kitazato[5]✉, Yifei Wang[1,2,3,4]✉, Zhe Ren[1,2,3,4]✉

Abstract

Microglia are the primary cellular source of type I interferons (I-IFNs) in the brain upon neurotropic virus infection. Although the I-IFN-based antiviral innate immune response is crucial for eliminating viruses, overproduction led to immune disorders. Therefore, the relatively long-lasting I-IFNs must be precisely controlled, but the regulatory mechanism for the innate antiviral response in microglia remains largely unknown. Long non-coding RNAs (lncRNAs) are being recognized as crucial factors in numerous diseases, but their regulatory roles in the innate antiviral response in microglia are undefined.

Methods: The high-throughput RNA sequencing was performed to obtain differentially expressed lncRNAs (DELs) in primary microglia infected with or without the neurotropic herpes simplex virus type 1 (HSV-1). We selected four DELs ranked in the top 15 in basic level and their fold change induced by HSV-1, i.e., FPKMHSV-1/FPKMCells.We subsequently found a key lncRNA affecting the innate antiviral response of microglia significantly. We next used dual-luciferase reporter assays, bioinformatical tools, and truncation mutants of both lncRNA and targeted proteins to elucidate the downstream and upstream mechanism of action of lncRNA. Further, we established microglia-specific knock-in (KI) mice to investigate the role of lncRNA in vivo.



Theranostics
2021 Sep 21 ; 11(19)
Impact Factor: 12.4

Materials and Methods

RNA-FISH was performed according to the protocol provided in the **RNA FISH Kit** (**GenePharma**). The **validated siRNAs** were obtained from Sigma and synthesized by **GenePharma**.

Redox Biology 66 (2023) 102858

Contents lists available at ScienceDirect

Redox Biology

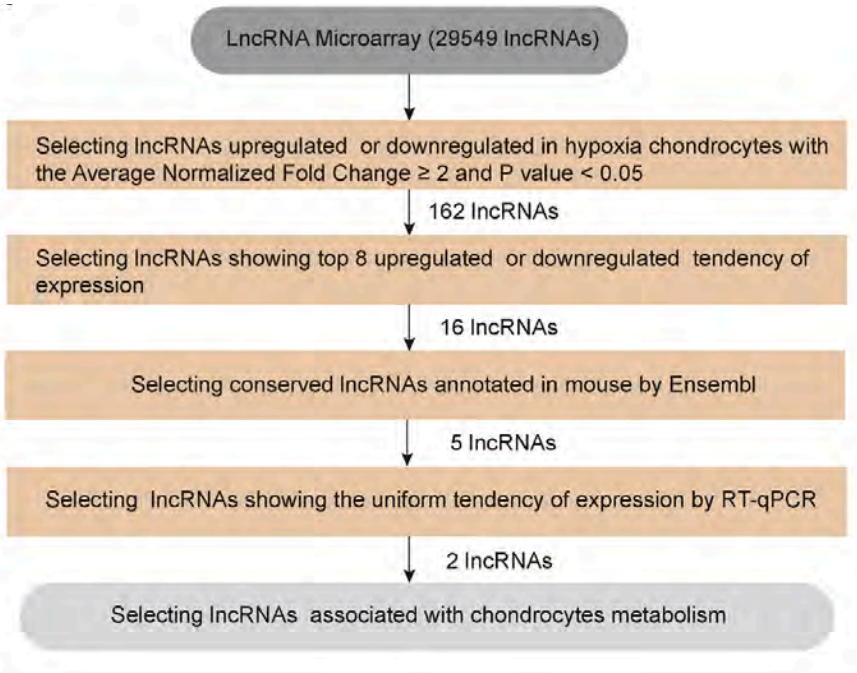
journal homepage: www.elsevier.com/locate/redox

An inducible long noncoding RNA, LncZFHX2, facilitates DNA repair to mediate osteoarthritis pathology

Weiyu Ni [a,b,1], Haitao Zhang [a,b,1], Zixuan Mei [a,b,1], Zhou Hongyi [a,b], Yizheng Wu [a,b], Wenbin Xu [a,b], Yan Ma [a,b], Wentao Yang [a,b], Yi Liang [a,b], Tianyuan Gu [a,b], Yingfeng Su [a,b], Shunwu Fan [a,b,**], Shuying Shen [a,b,***], Ziang Hu [a,b,*]

A B S T R A C T

Cartilage homeostasis is essential for chondrocytes to maintain proper phenotype and metabolism. Because adult articular cartilage is avascular, chondrocytes must survive in low oxygen conditions, and changing oxygen tension can significantly affect metabolism and proteoglycan synthesis in these cells. However, whether long noncoding RNA participate in cartilage homeostasis under hypoxia has not been reported yet. Here, we first identified LncZFHX2 as a lncRNA upregulated under physiological hypoxia in cartilage, specifically by HIF-1α. LncZFHX2 knockdown simultaneously accelerated cellular senescence, targeted multiple components of extra-cellular matrix metabolism, and increased DNA damage in chondrocytes. Through a series of *in vitro* and *in vivo* experiments, we identified that LncZFHX2 performed a novel function that regulated RIF1 expression through forming a transcription complex with KLF4 and promoting chondrocyte DNA repair. Moreover, chondrocyte- conditional knockout of LncZFHX2 accelerated injury-induced cartilage degeneration *in vivo*. In conclusion, we identified a hypoxia-activated DNA repair pathway that maintains matrix homeostasis in osteoarthritis cartilage.



Redox Biology
2023 Aug 19;66:102858
Impact Factor: 11.4

Materials and Methods

FISH signals were detected using a **FISH kit** (**GenePharma**, Jiangsu, China), according to the manufacturer's guidelines.

Biotinylated RNAs (**GenePharma**, Jiangsu, China) was incubated with 50 μL of streptavidin magnetic beads in RNA capture buffer at room temperature for 30 min.

Cao et al. Journal of Experimental & Clinical Cancer Research (2020) 39:102
https://doi.org/10.1186/s13046-020-01602-1

Journal of Experimental & Clinical Cancer Research

RESEARCH Open Access

Interplay between cancer cells and M2 macrophages is necessary for miR-550a-3-5p down-regulation-mediated HPV-positive OSCC progression

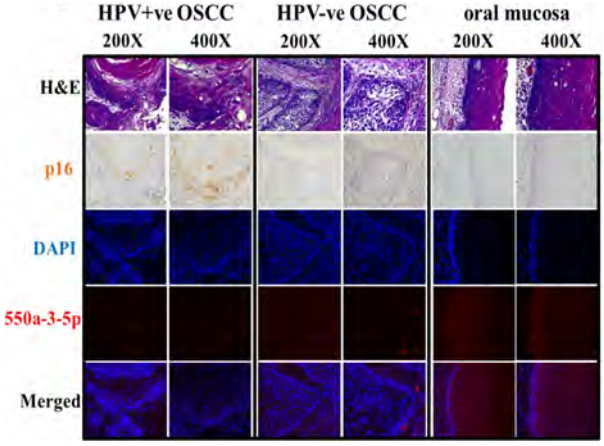
Ming-xin Cao[1], Wei-long Zhang[1], Xiang-hua Yu[1], Jia-shun Wu[1], Xin-wei Qiao[1], Mei-chang Huang[1], Ke Wang[1], Jing-biao Wu[1], Ya-Jie Tang[2], Jian Jiang[3], Xin-hua Liang[1*] and Ya-ling Tang[1*]

Abstract

Background: Human papillomavirus (HPV)-positive oral squamous cell carcinoma (OSCC) is increasing worldwide with typically higher grade and stage, while better prognosis. microRNAs (miRNAs) has been shown to play a critical role in cancer, however, their role in HPV-positive OSCC progression remains unclear.

Methods: miRNA microarray was performed to identify differentially expressed miRNAs. qRT-PCR and FISH were performed to determine the relative expression of miR-550a-3-5p. CCK-8, Flow cytometry, Wound healing, Cell invasion assays and xenograft experiments were conducted to analyze the biological roles of miR-550a-3-5p. Tumor-associated macrophages (TAMs) generation, co-culturing of cancer cells with TAMs, Western blot, Dual-luciferase reporter gene assay, Immunohistochemistry and animal studies were performed to explore the mechanisms underlying the functions of miR-550a-3-5p.

Results: We identified 19 miRNAs differentially expressed in HPV-positive OSCC specimens and miR-550a-3-5p was down-regulated. The low expression of miR-550a-3-5p correlated with higher tumor size and nodal metastasis of HPV-positive OSCC patients. Then, we found that miR-550a-3-5p suppressed the migration, invasion and EMT of HPV-positive OSCC cells dependent on decreasing M2 macrophages polarization. Moreover, miR-550a-3-5p, down-regulated by E6 oncoprotein, inhibited M2 macrophages polarization by YAP/CCL2 signaling, which in turn abrogating EMT program in HPV-positive OSCC cells. In addition, in both xenografts and clinical HPV-positive OSCC samples, miR-550a-3-5p levels were inversely associated with YAP, CCL2 expressions and the number of M2 macrophages.



Jornal of Experimental &Clinical Cancer Research
2020 Jun 3; 39:102
Impact Factor: 11.3

Materials and Methods
FISH assays were performed using **miRNA Fluorescence In Situ Hybridization Kit** (**GenePharma**).

Yang et al. Biomarker Research (2023) 11:59
https://doi.org/10.1186/s40364-023-00495-4

RESEARCH

Open Access

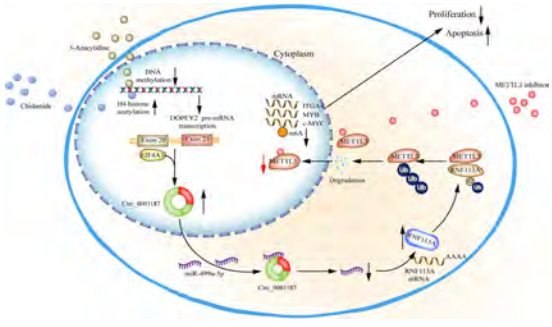
EIF4A3-induced Circ_0001187 facilitates AML suppression through promoting ubiquitin-proteasomal degradation of METTL3 and decreasing m6A modification level mediated by miR-499a-5p/RNF113A pathway

Xinyu Yang[1,2†], Fengjiao Han[1,2†], Xiang Hu[1,2], Guosheng Li[1,2], Hanyang Wu[1,2], Can Can[1,2], Yihong Wei[1,2], Jinting Liu[1,2], Ruiqing Wang[1,2], Wenbo Jia[1,2], Chunyan ji[1,2] and Daoxin Ma[1,2*]

Abstract

Aberrant expression of circRNAs has been proven to play a crucial role in the progression of acute myeloid leukemia (AML); however, its regulatory mechanism remains unclear. Herein, we identified a novel circRNA, Circ_0001187, which is downregulated in AML patients, and its low level contributes to a poor prognosis. We further validated their expression in large-scale samples and found that only the expression of Circ_0001187 was significantly decreased in newly diagnosed (ND) AML patients and increased in patients with hematological complete remission (HCR) com-pared with controls. Knockdown of Circ_0001187 significantly promoted proliferation and inhibited apoptosis of AML cells in vitro and in vivo, whereas overexpression of Circ _0001187 exerted the opposite effects. Interestingly, we found that Circ_0001187 decreases mRNA m^6A modification in AML cells by enhancing METTL3 protein degradation. Mechanistically, Circ_0001187 sponges miR-499a-5p to enhance the expression of E3 ubiquitin ligase RNF113A, which mediates METTL3 ubiquitin/proteasome-dependent degradation via K48-linked polyubiquitin chains. Moreover, we found that the low expression of Circ _0001187 is regulated by promoter DNA methylation and histone acetylation. Collectively, our findings highlight the potential clinical implications of Circ _0001187 as a key tumor suppressor in AML via the miR-499a-5p/RNF113A/METTL3 pathway

Biomarker Research
2023 Jun; 11: 59
Impact Factor:11.1



Materials and Methods

Hybridization was performed according to the manu-facturer's instructions using **a FISH Kit** (**GenePharma**, Shanghai, China).
The **miR-499a-5p mimics or inhibitor** and **related control oligonucleo-tides** were also precisely designed and provided by **GenePharma** (Shanghai, China).
The **siRNAs** of Circ_0001187, EIF4A3, RNF113A, METTL3, TRIM21, TRIM33, UBR5, MYCBP2, TRIM56, TRIM41, HUWE1, or HERC2 and their **related control oligonucleotides** were precisely designed and produced by **GenePharma** (Shanghai, China).
Mut-hsa-miR-499a-5p fragment was synthesized andinserted downstream of the luciferase reporter gene of the **pmirGLO Vector** (**GenePharma**, China).

ESC European Society of Cardiology
Cardiovascular Research (2023) **00**, 1–13
https://doi.org/10.1093/cvr/cvad077

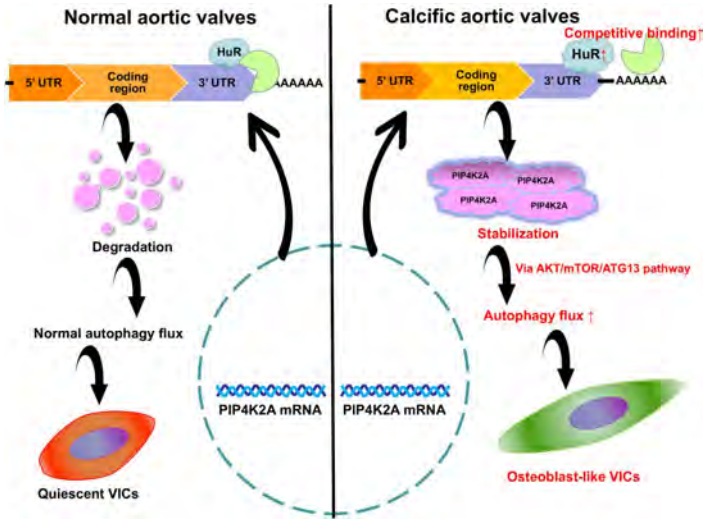
Human antigen R regulates autophagic flux by stabilizing autophagy-associated mRNA in calcific aortic valve disease

Juan Fang[1,2], Yi Qian[1,2,3], Jinyong Chen[1,2], Dilin Xu[1,2], Naifang Cao[1,2], Gangjie Zhu[1,2], Wangxing Hu[1,2], Haochang Hu[1,2], Ningjing Qian[1,2], Shuangshuang Yang[1,2], Jian'an Wang[1,2]*, and Xianbao Liu [1,2]*

Aims The incidence of calcific aortic valve disease (CAVD) has risen over the last decade and is expected to continue rising; however, pharmacological approaches have proven ineffective. In this study, we evaluated the role and underlying mechanisms of human antigen R (HuR)–mediated post-transcriptional regulation in CAVD.

Methods and results We found that HuR was significantly upregulated in human calcified aortic valves and primary aortic valvular interstitial cells (VICs) following osteogenic stimulation. Subsequent functional studies revealed that HuR silencing ameliorated calcification both *in vitro* and *in vivo*. For the first time, we demonstrated that HuR directly interacted with the transcript of phosphatidylinositol-5-phosphate 4-kinase, type II, alpha (PIP4K2A), which mediates phosphatidylinositol signalling, facilitates autophagy, and acts as an mRNA stabilizer. HuR positively modulated PIP4K2A expression at the post-transcriptional level and consequently influenced the AKT/mTOR/ATG13 pathway to regulate autophagy and CAVD progression.

Conclusion Our study provides new insights into the post-transcriptional regulatory role of HuR in modulating autophagy-positive factors to regulate the pathogenesis of CAVD. Our findings highlight the potential of HuR as an innovative therapeutic target in CAVD treatment.



CARDIOVASCULAR RESEARCH
2023 May 15 ;00:1-13
Impact Factor: 10.8

Materials and Methods

For transient transfections, hVICs at 70% confluency were treated with targeting **small interfering RNA (siRNA) or control siRNA** (**GenePharma**, Shanghai, China) at a concentration of 50 nM.
hVICs were seeded in six-well plates at a density of 1 × 105 cells per well and infected with lentiviruses at a multi-plicity of infection (MOI) of 50 in complete media containing 8 μg/mL **polybrene** (**GenePharma**). **A Cy3-labelled oligonucleotide probe** for PIP4K2A was designed and synthesized by **GenePharma**. RNA-FISH assays of aortic valve tissue sections were performed using a fluorescence in **situ hybridization kit** (**GenePharma**) according to the manufacturer's instructions.

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RESEARCH ARTICLE

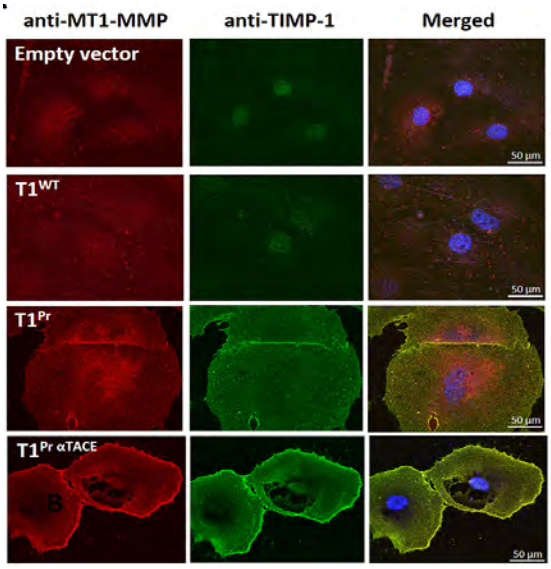
AMERICAN SOCIETY FOR MICROBIOLOGY | Molecular and Cellular Biology®

Translocating a High-Affinity Designer TIMP-1 to the Cell Membrane for Total Renal Carcinoma Inhibition: Putting the Prion Protein to Good Use

Bingjie Jiang,[a] Yuewei Xu,[b] Yihe Zhang,[a] Meng Huee Lee[a]

ABSTRACT Membrane type 1-matrix metalloproteinase (MT1-MMP) and tumor necrosis factor α (TNF-α)-converting enzyme (TACE) are prominent membrane-anchored metalloproteinases that regulate the turnover of extracellular matrix (ECM) components and bioactive molecules required for cancer proliferation. In this study, we describe a novel approach that would allow tissue inhibitor of metalloproteinase 1 (TIMP-1), the endogenous inhibitor of the matrix metallopro-teinases (MMPs), to be translocated to the cell membrane for simultaneous MT1-MMP/TACE inhibition. We achieve this by fusing $T1^{TACE}$, a designer TIMP-1 with superb affinities for MT1-MMP and TACE, to the glycosyl-phosphatidyl inositol anchor of prions to create a membrane-tethered, broad-spectrum inhibitor, named $T1^{Pr\ \alpha TACE}$, that colocalizes with MT1-MMP and TACE on the cell surface. Transduction of $T1^{Pr\ \alpha\ TACE}$ in human fibrosarcoma cells results not only in a sub-stantial reduction in gelatinolytic and TNF-α/heparin binding epithelial growth factor shedding activities but also in a loss of tubulogenic capability in three-dimensional matrices. In renal carcinoma, $T1^{Pr\ \alpha\ TACE}$ triggers cellular senescence and disrupts MMP-mediated proteolysis of ECM components such as fibronectin and collagen I, leading to an impairment in cell motility and survival under both *in vitro* and *in vivo* conditions. Taken together, our findings may provide a new perspective in TIMP targeting that could be exploited to halt metastatic renal carcinoma progression.

KEYWORDS ADAM, MMP, MT1-MMP, prion, TACE, TIMP



Molecular and Cellular Biology
2019 Aug 19;e00128-19
Impact Factor: 5.3

Materials and Methods
All experiments involving the use of **animals** were conducted by **GenePharma**, Co., Ltd.

Tang *et al. Molecular Cancer* (2024) 23:91
https://doi.org/10.1186/s12943-024-01998-w

RESEARCH Open Access

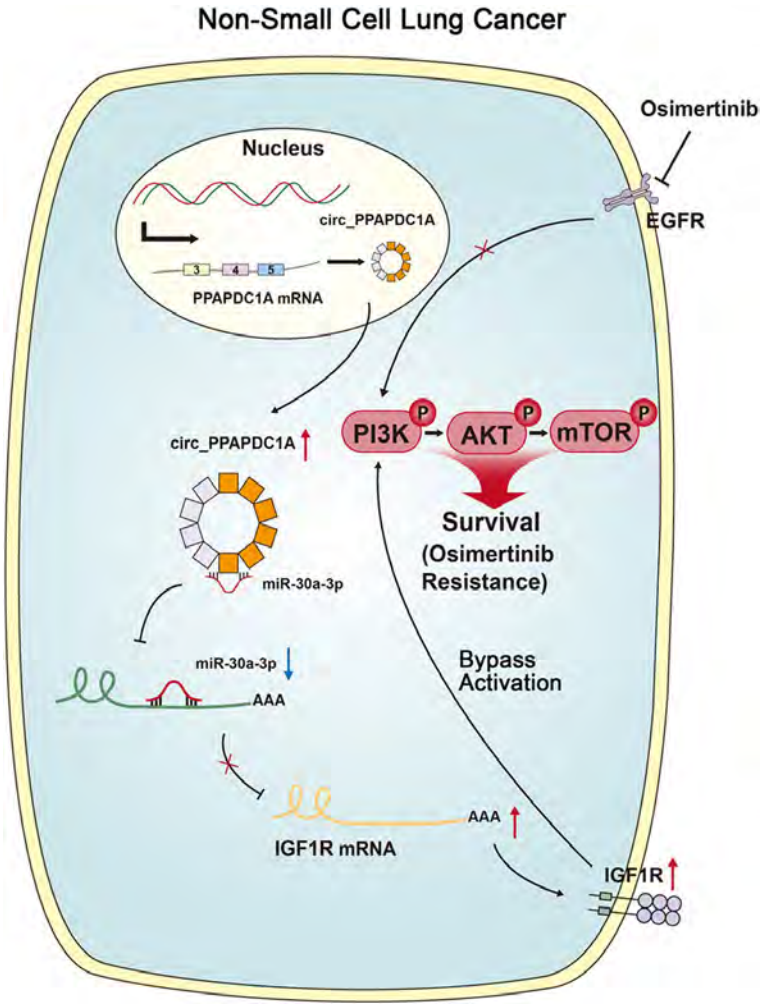
circ_PPAPDC1A promotes Osimertinib resistance by sponging the miR-30a-3p/ IGF1R pathway in non-small cell lung cancer (NSCLC)

Yi-fang Tang[1], Zheng-hua Liu[2], Lei-yi Zhang[3], Sheng-hao Shi[4], Shun Xu[2], Jin-An Ma[4], Chun-Hong Hu[4] and Fang-wen Zou[4*]

Abstract

Background Recent evidence has demonstrated that abnormal expression and regulation of circular RNA (circR- NAs) are involved in the occurrence and development of a variety of tumors. The aim of this study was to investigate the effects of circ_PPAPDC1A in Osimertinib resistance in NSCLC.

Methods Human circRNAs microarray analysis was conducted to identify differentially expressed (DE) circRNAs in Osimertinib-acquired resistance tissues of NSCLC. The effect of circ_PPAPDC1A on cell proliferation, invasion, migra- tion, and apoptosis was assessed in both in vitro and in vivo. Dual-luciferase reporter assay, RT-qPCR, Western-blot, and rescue assay were employed to confirm the interaction between circ_PPAPDC1A/miR-30a-3p/IGF1R axis.



Molecular Cancer Tang et al. Molecular Cancer (2024) 23:91
Impact Factor:37.3

Materials and Methods
Reporter plasmids containing **Wild-type (WT)** and **mutant (MUT) circ_PPAPDC1A (3'UTR) or IGF1R (IGF1R-WT and IGF1R-MUT) (3' UTR)** sequences were synthesized by Shanghai **Gene Pharma** Co

Molecular Cancer

RESEARCH Open Access

The circular RNA circSPARC enhances the migration and proliferation of colorectal cancer by regulating the JAK/STAT pathway

Jiaqi Wang[1,2†], Yi Zhang[1†], Hu Song[1†], Hang Yin[2], Tao Jiang[1], Yixin Xu[1], Lianyu Liu[1,2], Hongyu Wang[1,2], Hong Gao[2], Renhao Wang[1,2*] and Jun Song[1,2*]

Abstract

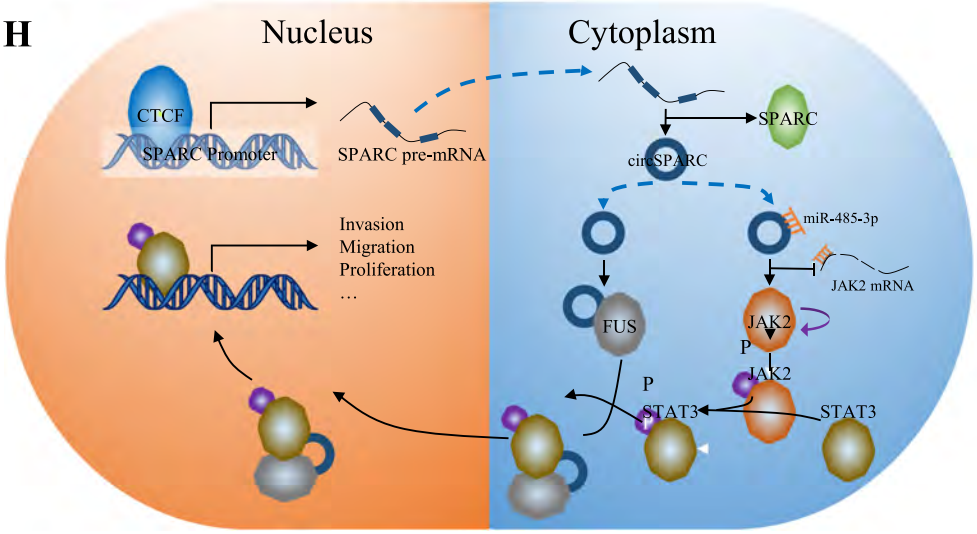
Background: Noncoding RNAs such as circular RNAs (circRNAs) are abundant in the human body and influence the occurrence and development of various diseases. However, the biological functions of circRNAs in colorectal cancer (CRC) are largely unknown.

Methods: RT-qPCR was used to detect the expression of circRNAs and mRNA in CRC cells and tissues. Fluorescence in situ hybridization (FISH) was used to analyze the location of circSPARC. Function-based experiments were performed using circSPARC knockdown and overexpression cell lines in vitro and in vivo, including CCK8, colony formation, transwell and metastasis models. Mechanistically, luciferase reporter assay, western blots, RNA, immunoprecipitation (RIP), Chromatin isolation by RNA purification (ChIRP) and immunohistochemical stainings were performed.

Results: CircSPARC was upregulated in both the tissues and plasma of CRC patients. High expression of circSPARC was associated with advanced TNM stage, lymph node metastases, and poor survival. Silencing circSPARC inhibited CRC cell migration and proliferation in vitro and vivo. Mechanistically, circSPARC sponged miR-485-3p to upregulate JAK2 expression and ultimately contribute to the accumulation of phosphorylated (p)-STAT3. Besides, circSPARC recruited FUS, which facilitated the nuclear translocation of p-STAT3.

Conclusions: These findings suggest that circSPARC might serve as a potential diagnostic and prognostic biomarker and a therapeutic target for CRC treatment by regulating JAK2/STAT3 pathway.

Keywords: Colorectal cancer, circRNA, circSPARC, JAK/STAT signalling pathway, Biomarker



Molecular Cancer
2021 Jun 1;20:81
Impact Factor: 37.3

Materials and Methods

The circSPARC sequence was cloned into the **psiCHECK-2** (**GenePharma**, China) vector, which contains the firefly luciferase gene (hLuc+) and Renilla luciferase gene (hRluc).

Molecular Cancer

RESEARCH Open Access

The circRNA circSEPT9 mediated by E2F1 and EIF4A3 facilitates the carcinogenesis and development of triple-negative breast cancer

Xiaying Zheng[1], Mengge Huang[2], Lei Xing[3], Rui Yang[1], Xiaosong Wang[1], Rong Jiang[4], Luyu Zhang[5] and Junxia Chen[1*]

Abstract

Background: Increasing studies have shown that circRNA is closely related to the carcinogenesis and development of many cancers. However, biological functions and the underlying molecular mechanism of circRNAs in triple-negative breast cancer (TNBC) remain largely unclear so far. **Methods:** Here, we investigated the expression pattern of circRNAs in four pairs of TNBC tissues and paracancerous normal tissues using RNA-sequencing. The expression and prognostic significance of circSEPT9 were evaluated with qRT-PCR and in situ hybridization in two TNBC cohorts. The survival curves were drawn by the Kaplan-Meier method, and statistical significance was estimated with the log-rank test. A series of in vitro and in vivo functional experiments were executed to investigate the role of circSEPT9 in the carcinogenesis and development of TNBC. Mechanistically, we explored the potential regulatory effects of E2F1 and EIF4A3 on biogenesis of circSEPT9 with chromatin immunoprecipitation (ChIP), luciferase reporter and RNA immunoprecipitation (RIP) assays. Furthermore, fluorescent in situ hybridization (FISH), luciferase reporter and biotin-coupled RNA pull-down assays were implemented to verify the relationship between the circSEPT9 and miR-637 inTNBC.

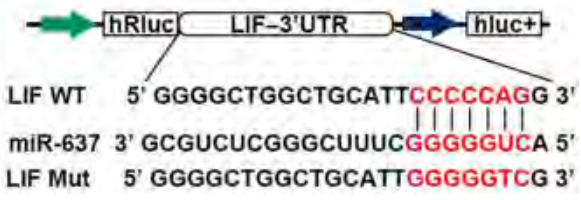
Molecular Cancer

2020 Apr 7 ; 19: 73

Impact Factor: 37.3

Materials and Methods

The sequences of circSEPT9 or LIF 3'UTR containing the wild-type (WT) or mutant (Mut) **binding site** of hsa-miR-637 were devised and synthesized by **GenePharma** (Shanghai, China).



Acta Pharmaceutica Sinica B xxxx;xxx(xxx):xxx

Chinese Pharmaceutical Association
Institute of Materia Medica, Chinese Academy of Medical Sciences

Acta Pharmaceutica Sinica B

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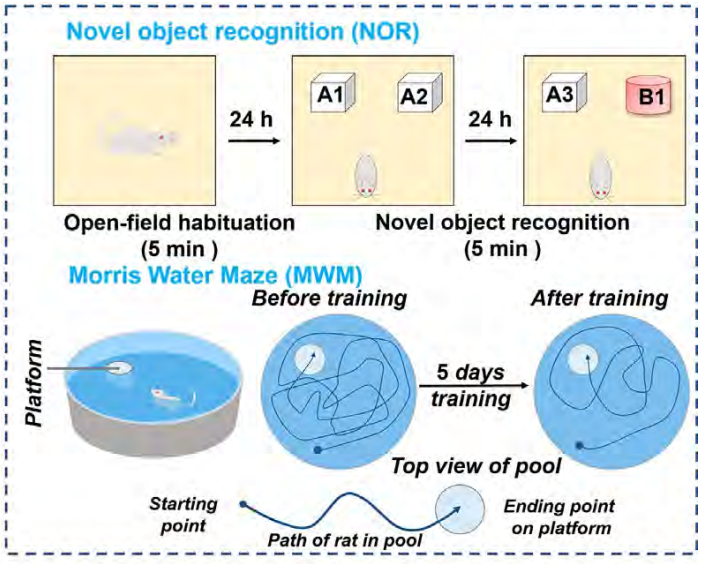
ORIGINAL ARTICLE

Gestational dexamethasone exposure impacts hippocampal excitatory synaptic transmission and learning and memory function with transgenerational effects

Mingcui Luo[a,c,†], Yiwen Yi[b,c,†], Songqiang Huang[b,c], Shiyun Dai[b,c], Lulu Xie[c,d], Kexin Liu[c,e], Shuai Zhang[a,c], Tao Jiang[b,c], Tingting Wang[a,c], Baozhen Yao[c,d], Hui Wang[b,c], Dan Xu[a,c,*]

Abstract The formation of learning and memory is regulated by synaptic plasticity in hippocampal neurons. Here we explored how gestational exposure to dexamethasone, a synthetic glucocorticoid commonly used in clinical practice, has lasting effects on offspring's learning and memory. Adult offspring rats of prenatal dexamethasone exposure (PDE) displayed significant impairments in novelty recognition and spatial learning memory, with some phenotypes maintained transgenerationally. PDE impaired synaptic transmission of hippocampal excitatory neurons in offspring of F1 to F3 generations, and abnormalities of neurotransmitters and receptors would impair synaptic plasticity and lead to impaired learning and memory, but these changes failed to carry over to offspring of F5 and F7 gener-ations. Mechanistically, altered hippocampal *miR-133a-3p*-SIRT1-CDK5-NR2B signaling axis in PDE multigeneration caused inhibition of excitatory synaptic transmission, which might be related to oocyte-specific high expression and transmission of *miR-133a-3p*. Together, PDE affects hippocampal



Acta Pharmaceutica Sinica B
2023 Mar ; 2211-3835
Impact Factor: 14.5

Materials and Methods
The **luciferase reporter plasmids** were constructed by **GenePharma** Technology (Shanghai, China).

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Theranostics

2021; 11(11): 5248-5266. doi: 10.7150/thno.54550

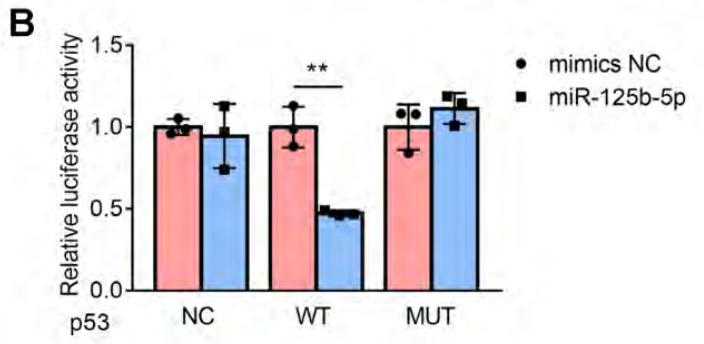
Research Paper

Exosomal miR-125b-5p deriving from mesenchymal stem cells promotes tubular repair by suppression of p53 in ischemic acute kidney injury

Jing-Yuan Cao[1*], Bin Wang[1*], Tao-Tao Tang[1*], Yi Wen[1], Zuo-Lin Li[1], Song-Tao Feng[1], Min Wu[1], Dan Liu[1], Di Yin[1], Kun-Ling Ma[1], Ri-Ning Tang[1], Qiu-Li Wu[1], Hui-Yao Lan[2], Lin-Li Lv[1]✉ and Bi-Cheng Liu[1]✉

Abstract: Mesenchymal stem cells-derived exosomes (MSC-exos) have attracted great interest as a cell-free therapy for acute kidney injury (AKI). However, the in vivo biodistribution of MSC-exos in ischemic AKI has not been established. The potential of MSC-exos in promoting tubular repair and the underlying mechanisms remain largely unknown.

Methods: Transmission electron microscopy, nanoparticle tracking analysis, and western blotting were used to characterize the properties of human umbilical cord mesenchymal stem cells (hucMSCs) derived exosomes. The biodistribution of MSC-exos in murine ischemia/reperfusion (I/R) induced AKI was imaged by the IVIS spectrum imaging system. The therapeutic efficacy of MSC-exos was investigated in renal I/R injury. The cell cycle arrest, proliferation and apoptosis of tubular epithelial cells (TECs) were evaluated in vivo and in HK-2 cells. The exosomal miRNAs of MSC-exos were profiled by high-throughput miRNA sequencing. One of the most enriched miRNA in MSC-exos was knockdown by transfecting miRNA inhibitor to hucMSCs. Then we investigated whether this candidate miRNA was involved in MSC-exos-mediated tubular repair.



Theranostics
2021 Mar 11;11(11):5248-5266.
Impact Factor: 12.4

Materials and Methods

HucMSCs were transfected with **miR-125b-5p inhibitor** or **negative control (NC) inhibitor** (**GenePharma**)

HK-2 cells were transfected with **siICAM-1** and **siVCAM-1** (**GenePharma**).

A plasmid containing P53 expression gene (pEX-P53) was constructed on a pEX-1 backbone (**GenePharma**).

Cy3-labeled probe sequences of miR-125b-5p were devised by **Genepharma** .

HK-2 cells were co-transfected with 3′UTR luciferase reporter constructs (3′UTR-NC, 3′UTR-TP53, 3′UTR-TP53-mutant), miRNA (miRNA-NC or miR-125b-5p), and Renilla luciferase using **GP-transfect-Mate** (**GenePharma**).

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Theranostics

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Research Paper

HIF-1-induced mitochondrial ribosome protein L52: a mechanism for breast cancer cellular adaptation and metastatic initiation in response to hypoxia

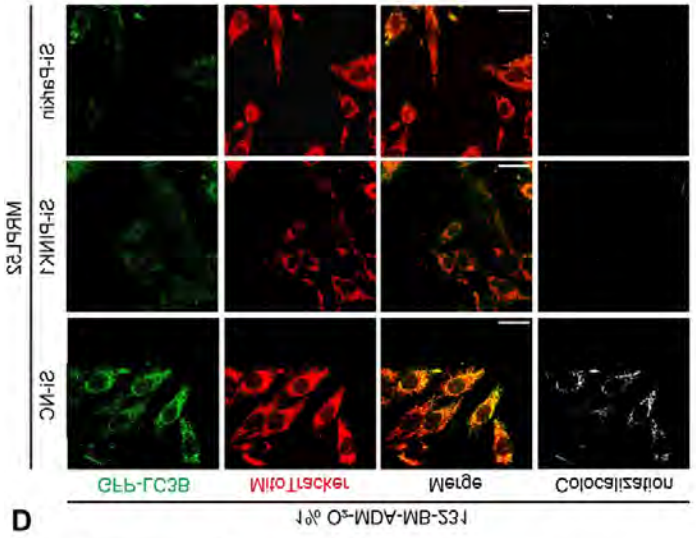
Xinyan Li[1#], Mengshen Wang[1#], Su Li[2], Yuqiong Chen[3], Mozhi Wang[1], Zhonghua Wu[4], Xiangyu Sun[1], Litong Yao[1], Haoran Dong[1], Yongxi Song[4✉], Yingying Xu[1✉]

Abstract

Background: Hypoxia is a hallmark of the physical microenvironment of solid tumors. As a key factor that regulates tumor development and progression, hypoxia can reprogram the expression of multiple genes, whose biological function and molecular mechanism in cancer remain largely unclear. The mitochondrial ribosome protein family consists of nuclear-encoded mitochondrial proteins that are responsible for protein synthesis in the mitochondria.

Methods: A high-throughput RNA sequencing assay was carried out to identify differentially expressed mRNAs between breast cancer tissues and adjacent normal tissues as well as breast tumors with metastasis and those without metastasis. Our clinical samples and TCGA database were analyzed to observe the clinical value of mitochondrial ribosome protein L52 (MRPL52) in human breast cancer. Potent hypoxia response elements in the promoter region of MRPL52 were identified and validated by chromatin immunoprecipitation and luciferase reporter assays. Functional experiments were performed using breast cancer cell lines with MRPL52 ectopic expression and knockdown cultured in a 20% or 1% O2 environment.

Conclusions: This work elucidates the molecular mechanism by which MRPL52 mediates hypoxia-induced apoptotic resistance and metastatic initiation of breast cancer, and provides new insights into the interplay between cancer and the tumor microenvironment.



Theranostics
2021 May 16; 11(15): 7337-7359
Impact Factor: 12.4

Materials and Methods

For construction of the luciferase reporter vectors of MRPL52, wild-type (WT) and mutant type (Mut) MRPL52 HREs were inserted into **firefly luciferase reporter vectors** (**GenePharma**, Shanghai, China). Lentiviruses were constructed by co-transfecting the 293T cell line with the **packaging plasmid Sh-MRPL52 (LV-Sh-MRPL52), MRPL52 (LV-MRPL52)** or **their negative control (LV-Sh-NC and LV-Vector)** (**GenePharma**, Shanghai, China).

THERANOSTICS
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PMID: 32483426

Non-canonical signaling pathway of SNAI2 induces EMT in ovarian cancer cells by suppressing miR-222-3p transcription and upregulating PDCD10

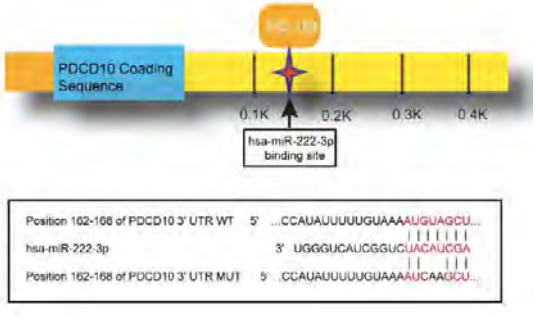
Abstract

Background: Epithelial ovarian cancer (EOC) is one of the most lethal malignancies in women worldwide. Many studies showed the transcription factor SNAI2-induced Epithelial-Mesenchymal Transition (EMT) through inhibiting E-cadherin (E-cad) expression. Our previous study reported that miR-222-3p was an important tumor-suppressive miRNA for EOC development and dissemination. The present study aimed to acquire a deeper mechanistic understanding of the role of miR-222-3p regulation that might contribute to improving current anti-metastasis strategies in EOC. **Methods:** A variety of techniques were used to measure mRNA and protein expression levels, including quantitative real-time polymerase chain reaction (qRT-PCR), Western blot, immunohistochemical (IHC) staining, and immunofluorescence (IF). Four different microRNA (miRNA) target prediction databases were used to predict the target genes of miR-222. Luciferase assay was performed to determine the direct binding of miR-222-3p to the untranslated region (3'-UTR) of PDCD10. The biological effects of PDCD10 and miR-222-3p were also investigated in vitro by Transwell and wound healing assays, as well as in vivo by a xenograft mice model. Combining UCSC and JASPAR, as well as ENCODE public databases, we predicted that the transcription factor SNAI2 could affect miR-222-3p expression. Luciferase assay was utilized to examine the validity of putative SNAI2 binding sites for miR-222-3p regulation. Chromatin immunoprecipitation (ChIP) was used to explore the SNAI2's occupancy on the miR-222-3p promoter.

Theranostice
2020 Apr 27 ; 10(13): 5895–5913
Impact Factor: 12.4

Materials and Methods

To construct the dual-luciferase reporter plasmid, PDCD10 luciferase vectors used in this study were cloned into **psiTM-Check2-control vector** (**GenePharma**, Shanghai, China) to create a wild-type (WT) psiTM-Check2-PDCD10-3'-UTR,which contained the predicted binding site of miR-222-3p on PDCD10's 3'-UTR (positions 162-168: AUGUAGC).



Li et al. Journal of Experimental & Clinical Cancer Research (2021) 40:168
https://doi.org/10.1186/s13046-021-01933-7

Journal of Experimental & Clinical Cancer Research

RESEARCH Open Access

SLC6A8-mediated intracellular creatine accumulation enhances hypoxic breast cancer cell survival via ameliorating oxidative stress

Qiao Li[1†], Manran Liu[1†], Yan Sun[2], Ting Jin[1], Pengpeng Zhu[1], Xueying Wan[1], Yixuan Hou[3] and Gang Tu[4*]

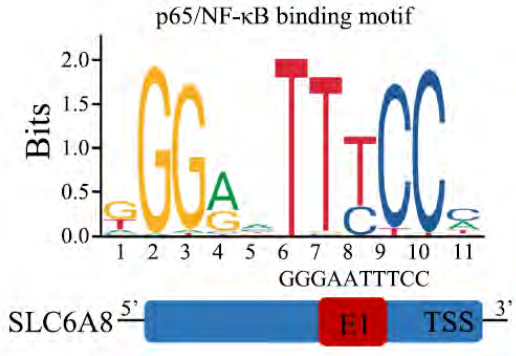
Abstract

Background: Triple-negative breast cancer (TNBC) is the most aggressive subtype of breast cancer, with poor prognosis and limited treatment options. Hypoxia is a key hallmark of TNBC. Metabolic adaptation promotes progression of TNBC cells that are located within the hypoxic tumor regions. However, it is not well understood regarding the precise molecular mechanisms underlying the regulation of metabolic adaptions by hypoxia.

Methods: RNA sequencing was performed to analyze the gene expression profiles in MDA-MB-231 cell line (20%O2 and 1% O2). Expressions of Slc6a8, which encodes the creatine transporter protein, were detected in breast cancer cells and tissues by quantitative real-time PCR. Immunohistochemistry was performed to detect SLC6A8 protein abundances in tumor tissues. Clinicopathologic correlation and overall survival were evaluated by chi-square test and Kaplan-Meier analysis, respectively. Cell viability assay and flow cytometry analysis with Annexin V/PI double staining were performed to investigate the impact of SLC6A8-mediated uptake of creatine on viability of hypoxic TNBC cells. TNBC orthotopic mouse model was used to evaluate the effects of creatine in vivo.

Conclusions: Our study indicates that SLC6A8-mediated creatine accumulation plays an important role in promoting TNBC progression, and may provide a potential therapeutic strategy option for treatment of SLC6A8 high expressed TNBC.

Keywords: SLC6A8, Creatine, Triple-negative breast cancer, Survival, Hypoxia



Journal of Experimental & Clinical Cancer Research
2021 May 14 ; 40:168
Impact Factor: 11.3

Materials and Methods

Short hairpin RNA (shRNA) oligonucleotides targeting Slc6a8, p65/NF-κB, HIF1A and HIF2A, and **control shRNA-NC** were all purchased from **GenePharma** (Shanghai, China). The promoter containing TP53/FOS/ETV4/p65/NF-κB-wild type binding sites (WT) or mutated binding sites (MUT) was cloned into pGL3 luciferase reporter vector to obtain the **pGL3/Slc6a8 WT reporter** and **pGL3/Slc6a8 MUT reporter** (**GenePharma**, China).

Jiang et al. *Cell Death and Disease* (2020)11:777
https://doi.org/10.1038/s41419-020-02978-w

ARTICLE Open Access

CCL18-induced LINC00319 promotes proliferation and metastasis in oral squamous cell carcinoma via the miR-199a-5p/FZD4 axis

Xiao Jiang[1], Jingpeng Liu[1], Simin Li[1], Bo Jia[1], Zhijie Huang[1], Jun Shen[1], Haiyun Luo[1] and Jianjiang Zhao[1]

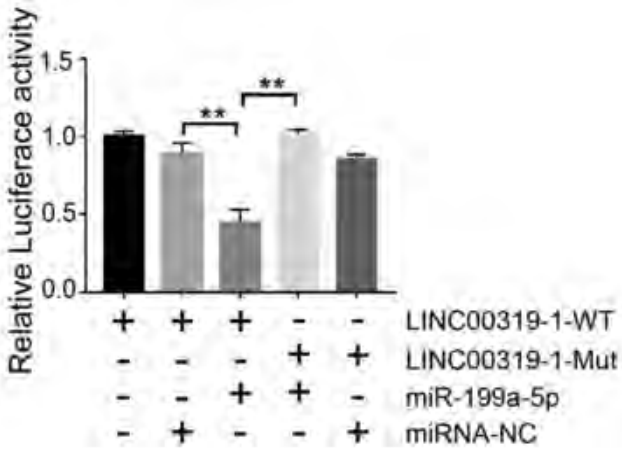
Abstract

Long non-coding RNAs (lncRNAs), which may be modulated by chemokines, are key regulators in many cancers including oral squamous cell carcinoma (OSCC). An understanding of lncRNAs involved in chemokine (CC motif) ligand 18 (CCL18)-induced OSCC promotion remains elusive. The present study using lncRNA sequencing found LINC00319 to be significantly upregulated in OSCC cells subjected to rCCL18 stimulation. Furthermore, LINC00319 knockdown was found to attenuate the carcinogenic function of CCL18 in OSCC, reducing OSCC proliferation, metastasis, epithelial-mesenchymal transition (EMT), and angiogenesis. LINC00319 was demonstrated to act as a ceRNA in OSCC, which directly responded to miR-199a-5p and rescued the repression of FZD4 by miR-199a-5p. Functionally, in vitro and in vivo experiments showed that LINC00319 promoted OSCC growth and metastasis via downregulating miR-199a-5p and upregulating FZD4. In vitro rescue assays demonstrated that miR-199a-5p inhibitor or FZD4 overexpression reversed the effects of LINC00319 silencing in OSCC. Importantly, the expression of miR-199a-5p and FZD4 were found to be mediated by CCL18, and miR-199a-5p mimics inhibited the CCL18-promoting effects in oral cancer cells. Taken together, these results evidenced a mechanism of CCL18 action in OSCC mediated through the LINC00319/miR-199a-5p/FZD4 signaling pathway, which may comprise a potential target for OSCC therapeutic development.

Cell Death & Disease
2020 Sep 18 ; 11: 777
Impact Factor: 9

Materials and Methods

Wild-type (WT) LINC00319, Mutant-type (MUT) LINC00319, WT-3′-UTR-FZD4 and MUT-3′-UTR-FZD4 were cloned into **PmirGLO vector** (**GenePharma**, China) to generate luciferase receptor plasmids (GenePharma, China).



Mei et al. *Cell Death and Disease* (2020)11:270
https://doi.org/10.1038/s41419-020-2487-z

Cell Death & Disease

ARTICLE Open Access

RNA methyltransferase NSUN2 promotes gastric cancer cell proliferation by repressing $p57^{Kip2}$ by an m^5C-dependent manner

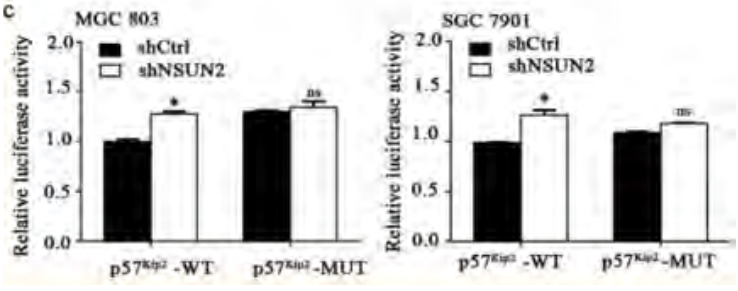
Lin Mei[1], Cheng Shen[1], Ran Miao[2], Jing-Zi Wang[3], Mend-Da Cao[3], Yi-Sheng Zhang[1], Liang-Hui Shi[1], Guo-Hai Zhao[1], Ming-Hai Wang[1], Li-Sheng Wu[2] and Ji-Fu Wei[3]

Abstract

The RNA methyltransferase NSUN2 has been involved in the cell proliferation and senescence, and is upregulated in various types of cancers. However, the role and potential mechanism of NSUN2 in gastric cancer remains to be determined. Our study showed that NSUN2 was significantly upregulated in gastric cancers, compared to adjacent normal gastric tissues. Moreover, NSUN2 could promote gastric cancer cell proliferation both in vitro and in vivo. Further study demonstrated that CDKN1C ($p57^{Kip2}$) was the potential downstream gene of regulated by NSUN2 in gastric cancer. NSUN2 could promote gastric cancer cell proliferation through repressing $p57^{Kip2}$ in an m^5C-dependent manner. Our findings suggested that NSUN2 acted as an oncogene through promoting gastric cancer development by repressing $p57^{Kip2}$ in an m^5C-dependent manner, which may provide a novel therapeutic target against gastric cancer.

Cell Death & Disease
2020 Sep 18 ; 11: 777
Impact Factor: 9

Materials and Methods
Wild-type and mutant 3′-UTR of p57Kip2 reporter plasmid were constructed from **GenePharma**.



Am J Cancer Res 2019;9(9):1938-1956
www.ajcr.us /ISSN:2156-6976/ajcr0100301

Original Article

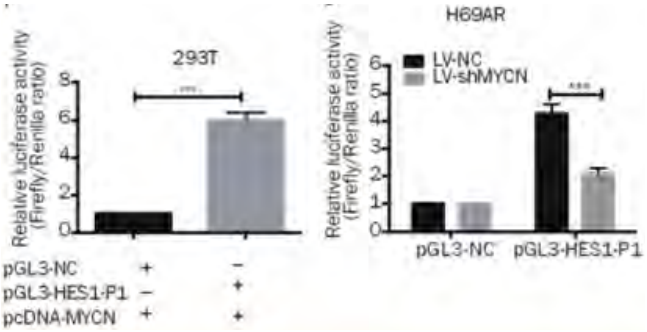
MYCN-mediated regulation of the HES1 promoter enhances the chemoresistance of small-cell lung cancer by modulating apoptosis

Abstract: MYCN, a member of the MYC family, is correlated with tumorigenesis, metastasis and therapy in many malig nancies; however, its role in small-cell lung cancer (SCLC) remains unclear. In this study, we sought to identify the function of MYCN in SCLC chemoresistance and found that MYCN is overexpressed in chemoresistant SCLC cells. We used MYCN gain- and loss-of- function experiments to demonstrate that MYCN promotes in vitro and in vivo chemoresistance in SCLC by inhibiting apoptosis. Mechanistic investigations showed that MYCN binds to the HES1 promoter and exhibits transcriptional activity. Furthermore, MYCN mediated SCLC chemoresistance through HES1. Accordingly, the NOTCH inhibitor FLI-60 derepressed HES1 and diminished MYCN-induced chemoresistance in SCLC. Finally, the positive correlation between HES1 and MYCN was confirmed in SCLC patients. Chemoresistant SCLC patients had higher expression levels of MYCN and HES1 than patients without chemoresistant SCLC. MYCN overexpression was related to advanced clinical stage and shorter survival in SCLC. In conclusion, our study revealed that MYCN and HES1 may be potential therapeutic targets and promising predictors for SCLC.

American Journal of Cancer Research
2019 Sep 15 ; 9(9):1938-1956
Impact Factor: 5.3

Materials and Methods

The pGL3-basic vector (Promega) and **pRL-TK vector** (**GenePharma**) were purchased. The pGL3-basic-promoter (pGL3-HES1-P1) and negative control (pGL3-NC) plasmids were constructed by inserting the HES1 promoter region or negative control region into the pGL3-basic plasmid; the **plasmids** were constructed by **GenePharma** (Shanghai, China).



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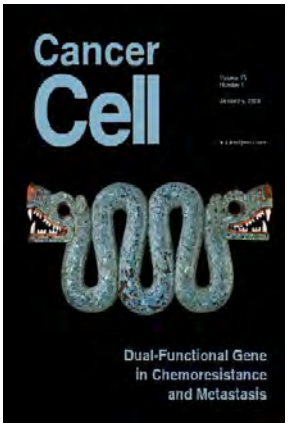
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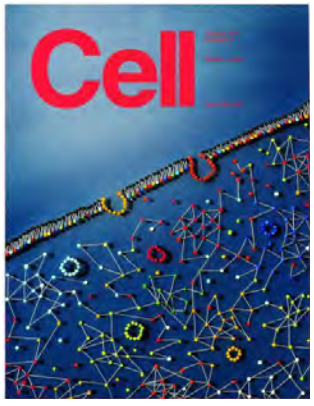
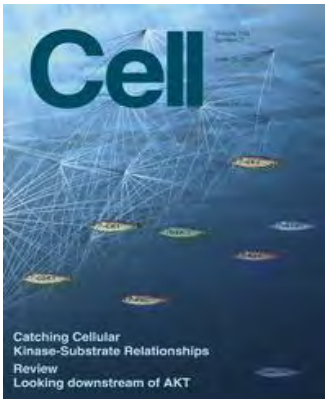
Dual-Functional Gene in Chemoresistance and Metastasis


Cell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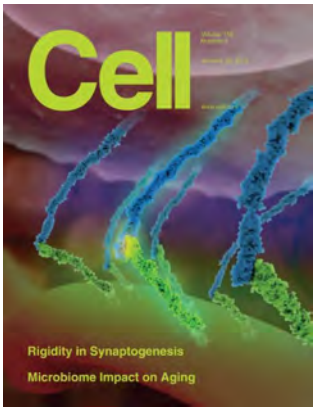
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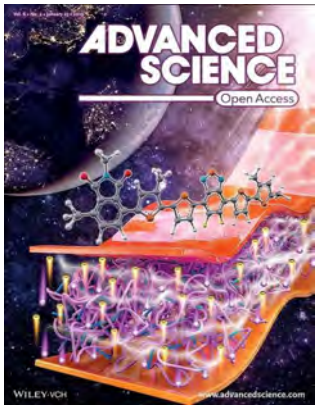
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