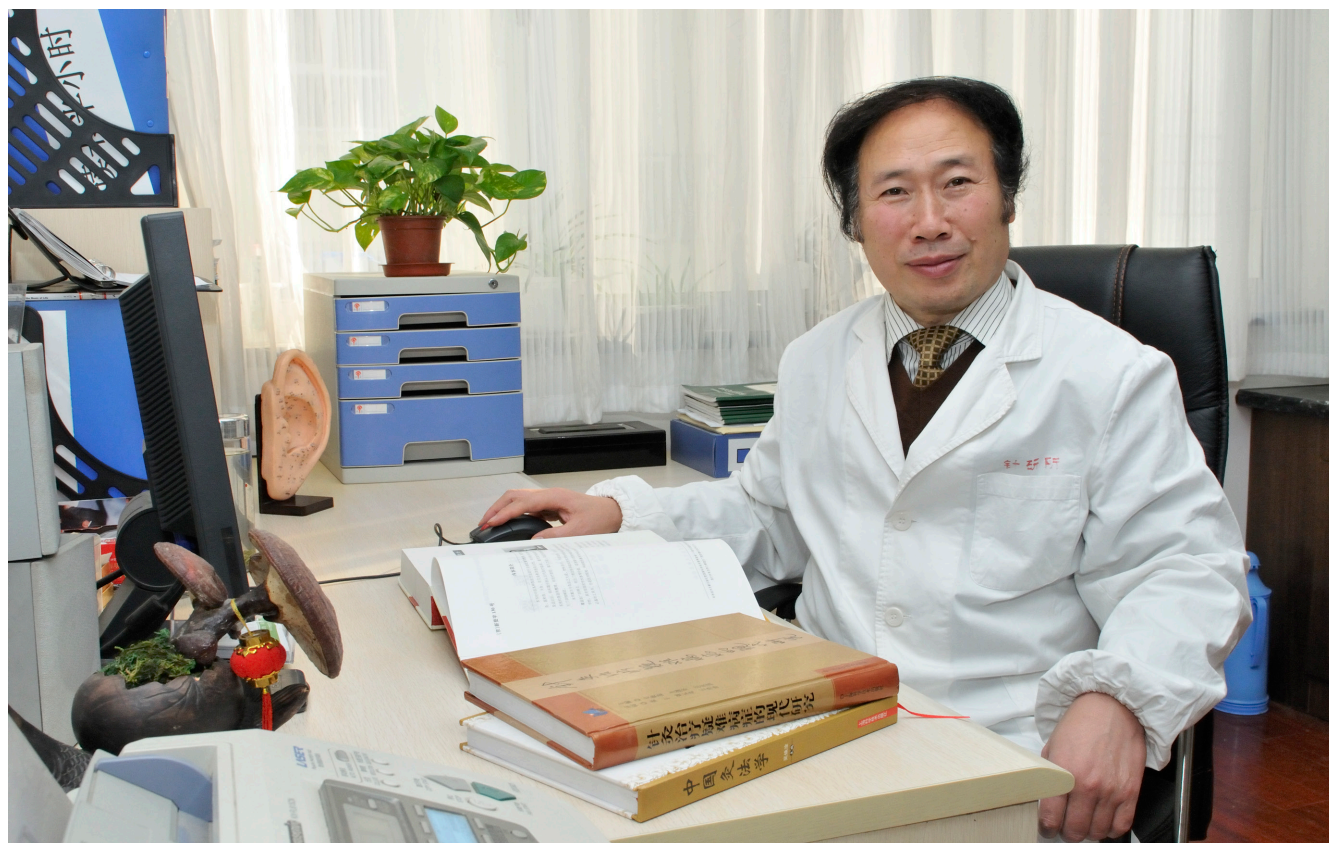


# 世界华人消化杂志®

**WORLD CHINESE  
JOURNAL OF DIGESTOLOGY**

**Shijie Huaren Xiaohua Zazhi**

2021 年 10 月 8 日      第 29 卷      第 19 期      (Volume 29 Number 19)



**19/2021**

ISSN 1009-3079



9 771009 307056

《世界华人消化杂志》是一本高质量的同行评议、开放获取和在线出版的学术刊物。本刊被国际检索系统《化学文摘(Chemical Abstracts, CA)》、《医学文摘库/医学文摘(EMBASE/Excerpta Medica, EM)》、《文摘杂志(Abstract Journal, AJ)》、Scopus、中国知网《中国期刊全文数据库(CNKI)》、《中文科技期刊数据库(CSTJ)》和《超星期刊域出版平台(Superstar Journals Database)》数据库收录。



### 文献综述

- 1089 抗栓治疗消化道损伤的中西医防治研究进展  
蚁楷宏, 谭学瑞
- 1096 长链非编码RNA调控胃癌巨噬细胞极化研究进展  
锁瑞洋, 王芝徐, 王健生, 张广健, 张佳
- 1102 短链脂肪酸与肠易激综合征关系的研究进展  
杭露, 周盐, 孟杨杨, 冯雅, 王殷姝, 袁建业

### 临床研究

- 1110 非选择性 $\beta$ 受体阻滞剂对晚期慢性肝病炎症因子及预后的影响  
王艳娇, 朱雅碧, 魏雯佳
- 1118 肝细胞癌中CBX2的免疫和预后意义的综合分析  
宋鑫, 王添贤, 朱小年, 谭盛葵

### 临床实践

- 1130 嗜酸乳杆菌联合莫沙必利治疗颅脑损伤术后胃肠功能障碍的临床研究  
金蓓, 罗凤飞
- 1138 遗传性大肠癌患者一级亲属肿瘤早治疗意识现况及其相关因素分析  
王会杰, 王建华, 徐丹, 王娜
- 1144 基于微信平台以TTM为导向的健康宣教法对溃疡性结肠炎患者正性情感、负性情感及自护能力的影响  
卓丽丽, 诸葛玮玮, 丁银蓉

## 消 息

- 1095 《腹痛的诊断、鉴别诊断与治疗》书讯
- 1109 《世界华人消化杂志》正文要求
- 1137 《世界华人消化杂志》修回稿须知
- 1150 《世界华人消化杂志》栏目设置

## 封面故事

吴焕淦, 上海中医药大学首席教授, 博导, 中国针灸学会副会长, 上海市针灸学会会长, 2项国家“973计划”针灸项目首席科学家, 国务院政府特殊津贴专家, 卫生部有突出贡献中青年专家, 上海市名中医, 上海市针灸经络研究所所长, 国家中管局针灸免疫效应重点研究室主任, 研究方向为针灸作用的基本原理与应用规律研究。以第一完成人获国家科技进步二等奖一项、2017年度上海市科技进步一等奖一项、2019年度教育部科技进步奖一等奖一项。

## 本期责任人

编务 张砚梁; 送审编辑 张砚梁; 组版编辑 张砚梁; 英文编辑 王天奇;  
形式规范审核编辑部主任 李香; 最终清样审核总编辑 马连生

## 世界华人消化杂志

Shijie Huaren Xiaohua Zazhi

吴阶平 题写封面刊名

陈可冀 题写版权刊名

(半月刊)

创 刊 1993-01-15

改 刊 1998-01-25

出 版 2021-10-08

原刊名 新消化病学杂志

期刊名称

世界华人消化杂志

国际标准连续出版物号

ISSN 1009-3079 (print) ISSN 2219-2859 (online)

主编

党双锁, 教授, 710004, 陕西省西安市, 西安交通大学医学院第二附属医院感染科

江学良, 教授, 250031, 山东省济南市, 中国人民解放军济南军区总医院消化科

刘占举, 教授, 200072, 上海市, 同济大学附属第十人民医院消化内科

吕宾, 教授, 310006, 浙江省杭州市, 浙江中医药大学附属医院(浙江省中医院)消化科

马大烈, 教授, 200433, 上海市, 中国人民解放军第二军医大学附属长海医院病理科

王俊平, 教授, 030001, 山西省太原市, 山西省人民医院消化科

王小众, 教授, 350001, 福建省福州市, 福建医科大学附属协和医院消化内科

姚登福, 教授, 226001, 江苏省南通市, 南通大学附属医院临床医学研究中心

张宗明, 教授, 100073, 北京市, 首都医科大学北京电力医院普外科

编辑委员会

编辑委员会成员在线名单, 详见:

<https://www.wjgnet.com/1009-3079/editorialboard.htm>

编辑部

王金磊, 主任

《世界华人消化杂志》编辑部

Baishideng Publishing Group Inc

7041 Koll Center Parkway, Suite 160, Pleasanton,

CA 94566, USA

Telephone: +1-925-3991568

E-mail: [wcjd@wjgnet.com](mailto:wcjd@wjgnet.com)<http://www.wjgnet.com>

出版

百世登出版集团有限公司

Baishideng Publishing Group Inc

7041 Koll Center Parkway, Suite 160, Pleasanton,

CA 94566, USA

Telephone: +1-925-3991568

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)<https://www.wjgnet.com>

制作

北京百世登生物医学科技有限公司  
100025, 北京市朝阳区东四环中路  
62号, 远洋国际中心D座903室  
电话: +86-10-85381892

《世界华人消化杂志》是一本高质量的同行评议, 开放获取和在线出版的学术刊物。本刊被国际检索系统《化学文摘(Chemical Abstracts, CA)》、《医学文摘库/医学文摘(EMBASE/Excerpta Medica, EM)》、《文摘杂志(Abstract Journal, AJ)》、Scopus、中国知网《中国期刊全文数据库(CNKI)》、《中文科技期刊数据库(CSTJ)》和《超星期刊出版平台(Superstar Journals Database)》数据库收录。

《世界华人消化杂志》正式开通了在线办公系统(<https://www.baishideng.com>), 所有办公流程一律可以在线进行, 包括投稿、审稿、编辑、审读, 以及作者、读者和编者之间的信息反馈交流。

特别声明

本刊刊出的所有文章不代表本刊编辑部和本刊编委会的观点, 除非特别声明。本刊如有印装质量问题, 请向本刊编辑部调换。

定价

每期136.00元 全年24期3264.00元

© 2021 Baishideng Publishing Group Inc. All rights reserved.



REVIEW

- 1089 Advances in prevention and treatment of digestive tract damage induced by antithrombotic therapy with traditional Chinese and Western medicine  
*Yi KH, Tan XR*
- 1096 Role of long non-coding RNA in regulating polarization of gastric cancer macrophages  
*Suo RY, Wang ZY, Wang JS, Zhang GJ, Zhang J*
- 1102 Progress in understanding of relationship between short chain fatty acids and irritable bowel syndrome  
*Hang L, Zhou Y, Meng YY, Feng Y, Wang YS, Yuan JY*

CLINICAL RESEARCH

- 1110 Effect of non-selective  $\beta$ -receptor blockers on inflammatory factors and prognosis in advanced chronic liver disease  
*Wang YJ, Zhu YB, Wei WJ*
- 1118 Immunological and prognostic significance of CBX2 expression in hepatocellular carcinoma  
*Song X, Wang TX, Zhu XN, Tan SK*

CLINICAL PRACTICE

- 1130 Clinical effects of *Lactobacillus acidophilus* combined with mosapride in treatment of gastrointestinal dysfunction after craniocerebral injury  
*Jin B, Luo FF*
- 1138 Awareness regarding early treatment and related factors in first-degree relatives of patients with hereditary colorectal cancer  
*Wang HJ, Wang JH, Xu D, Wang N*
- 1144 Impact of TTM-oriented health promotion and education method based on WeChat platform on positive emotions, negative emotions, and self-care ability of patients with ulcerative colitis  
*Zhuo LL, Zhuge WW, Ding YR*



## Contents

*World Chinese Journal of Digestology*  
Volume 29 Number 19 October 8, 2021

### COVER

Editorial Board Member of *World Chinese Journal of Digestology*, Huan-Gan Wu, Professor, Shanghai Research Institute of Acupuncture and Meridian, Shanghai University of Traditional Chinese Medicine, No.650 Wanping South Road, Xuhui District, Shanghai 200030, China. wuhuangan@126.com

### Indexed/Abstracted by

Chemical Abstracts, EMBASE/Excerpta Medica, Abstract Journals, Scopus, CNKI, CSTJ and Superstar Journals Database.

### RESPONSIBLE EDITORS FOR THIS ISSUE

Assistant Editor: *Yan-Liang Zhang*

Review Editor: *Yan-Liang Zhang*

Production Editor: *Yan-Liang Zhang*

English Language Editor: *Tian-Qi Wang*

Proof Editor: *Xiang Li*

Layout Reviewer: *Lian-Sheng Ma*

### Shijie Huaren Xiaohua Zazhi

**Founded** on January 15, 1993

**Renamed** on January 25, 1998

**Publication date** October 8, 2021

#### NAME OF JOURNAL

*World Chinese Journal of Digestology*

#### ISSN

ISSN 1009-3079 (print) ISSN 2219-2859 (online)

#### EDITOR-IN-CHIEF

**Shuang-Suo Dang, Professor**, Department of Infectious Diseases, the Second Affiliated Hospital of Medical School of Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China

**Xue-Liang Jiang, Professor**, Department of Gastroenterology, General Hospital of Jinan Military Command of Chinese PLA, Jinan 250031, Shandong Province, China

**Zhan-Ju Liu, Professor**, Department of Gastroenterology, Shanghai Tenth People's Hospital, Tongji University, Shanghai 200072, China

**Bin Lv, Professor**, Department of Gastroenterology, the First Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou 310006, Zhejiang Province, China

**Da-Lie Ma, Professor**, Department of Pathology, Changhai Hospital, the Second Military Medical University of Chinese PLA, Shanghai 200433, China

**Jun-Ping Wang, Professor**, Department of Gastroenterology, People's Hospital of Shanxi,

Taiyuan 030001, Shanxi Province, China

**Xiao-Zhong Wang, Professor**, Department of Gastroenterology, Union Hospital, Fujian Medical University, Fuzhou 350001, Fujian Province, China

**Deng-Fu Yao, Professor**, Clinical Research Center, Affiliated Hospital of Nantong University, Nantong 226001, Jiangsu Province, China

**Zong-Ming Zhang, Professor**, Department of General Surgery, Beijing Electric Power Hospital, Capital Medical University, Beijing 100073, China

#### EDITORIAL BOARD MEMBERS

All editorial board members resources online at <https://www.wjgnet.com/1009-3079/editorialboard.htm>

#### EDITORIAL OFFICE

Jin-Lei Wang, Director

*World Chinese Journal of Digestology*

Baishideng Publishing Group Inc

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: [wjcd@wjgnet.com](mailto:wjcd@wjgnet.com)

<https://www.wjgnet.com>

#### PUBLISHER

Baishideng Publishing Group Inc

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

<https://www.wjgnet.com>

### PRODUCTION CENTER

Beijing Baishideng BioMed Scientific Co., Limited Room 903, Building D, Ocean International Center, No. 62 Dongsihuan Zhonglu, Chaoyang District, Beijing 100025, China  
Telephone: +86-10-85381892

### PRINT SUBSCRIPTION

RMB 136 Yuan for each issue

RMB 3264 Yuan for one year

### COPYRIGHT

© 2021 Baishideng Publishing Group Inc. Articles published by this open access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

### SPECIAL STATEMENT

All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, but not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

### INSTRUCTIONS TO AUTHORS

Full instructions are available online at <https://www.wjgnet.com/1009-3079/Nav/36>. If you do not have web access, please contact the editorial office.

# 长链非编码RNA调控胃癌巨噬细胞极化研究进展

锁瑞洋, 王芝徐, 王健生, 张广健, 张佳

锁瑞洋, 王芝徐, 王健生, 张广健, 张佳, 西安交通大学第一附属医院  
胸外科 陕西省西安市 710061

锁瑞洋, 王芝徐, 西安交通大学医学部 陕西省西安市 710061

锁瑞洋, 研究方向为西安交通大学临床医学本科在读, 研究方向为肺癌和食管癌治疗、单孔腹腔镜应用和改进。

基金项目: 国家自然科学基金青年项目, No.81702430.

作者贡献分布: 锁瑞洋主要完成相关资料检索、分析以及论文的撰写; 王芝徐主要负责文章的投稿和修改; 王健生和张广健教授主要对文章内容进行评价和修改; 张佳教授主要负责文章构思、稿件修改、指导论文写作。

通讯作者: 张佳, 博士, 副主任医师, 710061, 陕西省西安市雁塔西路277号, 西安交通大学第一附属医院胸外科. [zhangjiaxjtu@xjtu.edu.cn](mailto:zhangjiaxjtu@xjtu.edu.cn)

收稿日期: 2021-05-11

修回日期: 2021-06-06

接受日期: 2021-08-24

在线出版日期: 2021-10-08

## Role of long non-coding RNA in regulating polarization of gastric cancer macrophages

Rui-Yang Suo, Zhi-Yu Wang, Jian-Sheng Wang, Guang-Jian Zhang, Jia Zhang

Rui-Yang Suo, Zhi-Yu Wang, Jian-Sheng Wang, Guang-Jian Zhang, Jia Zhang, Department of Thoracic Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Rui-Yang Suo, Zhi-Yu Wang, Xi'an Jiaotong University Health Science Center, Xi'an 710061, China

Supported by: National Natural Scientific Foundation of China, No.81702430.

Corresponding author: Jia Zhang, PhD, Associate Chief Physician, Department of Thoracic Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, No. 277 Yanta West Road, Xi'an 710061, Shaanxi Province, China. [zhangjiaxjtu@xjtu.edu.cn](mailto:zhangjiaxjtu@xjtu.edu.cn)

Received: 2021-05-11

Revised: 2021-06-06

Accepted: 2021-08-24

Published online: 2021-10-08

## Abstract

Tumor-associated macrophages (TAMs) are an important part of the tumor microenvironment. They are distributed in tumor tissues and distant metastatic sites, and are related to tumor progression and prognosis. TAMs M2 can promote tumor biological processes such as tumor proliferation, invasion, and metastasis, and inhibit apoptosis, and are obviously related to the poor prognosis of tumor patients. In recent years, the role of long non-coding RNAs (lncRNAs) in regulating the polarization of macrophages has gradually been revealed, which can affect the occurrence and development of tumors by adjusting the polarization of macrophages. Studies have shown that lncRNAs play an important role in the polarization process of gastric cancer macrophages. This article summarizes the related research reports, hoping to provide ideas for studies that interfere with the polarization process of TAMs to inhibit tumor progression.

© The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Key Words: Gastric cancer; Macrophages; Tumor microenvironment; lncRNAs

Citation: Suo RY, Wang ZY, Wang JS, Zhang GJ, Zhang J. Role of long non-coding RNA in regulating polarization of gastric cancer macrophages. *Shijie Huaren Xiaohua Zazhi* 2021; 29(19): 1096-1101

URL: <https://www.wjgnet.com/1009-3079/full/v29/i19/1096.htm>

DOI: <https://dx.doi.org/10.11569/wcjd.v29.i19.1096>

## 摘要

肿瘤相关巨噬细胞(Tumor-associated macrophages, TAMs)是肿瘤微环境重要的组成部分, 其在肿瘤组织和远处转移部位均有分布, 与肿瘤的进展和预后有关。

关. M2型TAMs可促进肿瘤增殖、侵袭转移、抑制凋亡等肿瘤生物学过程, 与肿瘤患者的不良预后明显相关. 近年来, 长链非编码RNA (long non-coding RNAs, lncRNAs)调控巨噬细胞极化的作用逐渐被揭示, 其可通过调控巨噬细胞极化方向来影响肿瘤的发生和发展. 研究表明lncRNAs在胃癌巨噬细胞极化过程发挥重要作用, 现就相关研究报道进行综述, 以期干预TAMs极化过程抑制胃癌进展的相关研究提供思路.

© The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

关键词: 胃癌; 巨噬细胞; 肿瘤微环境; 长链非编码RNA

**核心提要:** 近年来的研究发现长链非编码RNA (long non-coding RNAs, lncRNAs)参与了巨噬细胞的极化过程, 影响肿瘤的进展和预后. 本文就lncRNAs调控胃癌巨噬细胞极化的研究进展进行了概括.

**文献来源:** 锁瑞洋, 王芝徐, 王健生, 张广健, 张佳. 长链非编码RNA调控胃癌巨噬细胞极化研究进展. 世界华人消化杂志 2021; 29(19): 1096-1101

**URL:** <https://www.wjgnet.com/1009-3079/full/v29/i19/1096.htm>

**DOI:** <https://dx.doi.org/10.11569/wjcd.v29.i19.1096>

## 0 引言

胃癌是一类消化系统的恶性肿瘤, 是全球第五大恶性肿瘤, 也是全球癌症死亡相关的第二大原因<sup>[1]</sup>. 由于饮食习惯、幽门螺杆菌感染率高等因素, 中国是胃癌的高发国家, 尽管早期胃癌内镜下筛查已经取得了一定的效果, 但是大约35%的胃癌发现时已发生远处转移, 且转移性胃癌5年生存率仅为5%-20%<sup>[2,3]</sup>. 晚期肿瘤患者失去手术机会, 目前晚期胃癌主要治疗方法包括放化疗、分子靶向和免疫治疗, 截止目前仍未取得理想的效果. 肿瘤相关巨噬细胞(tumor-associated macrophage, TAMs)被认为是肿瘤微环境的重要组成部分, 易受局部微环境信号对其影响而发生极化. 长链非编码RNA (long non-coding RNA, lncRNAs)是广泛存在于机体内的一段超过200个核苷酸的不编码蛋白质的RNA分子, 近年来的研究发现其参与了巨噬细胞极化过程, 影响肿瘤的进展和预后. 胃癌初期症状大多比较隐蔽, 很难早期诊断<sup>[4]</sup>. 因此寻找其特异性的生物标志物并依据其开发新的诊断、治疗方法对胃癌诊治具有重要意义.

## 1 巨噬细胞极化

研究表明, 胃癌的侵袭和转移与肿瘤微环境(tumor microenvironment, TME)密切相关, 肿瘤与环境相互依存, 相互影响<sup>[5]</sup>. TME指肿瘤生长的特殊环境, 由血管内皮细胞、免疫细胞等一系列细胞构成, TAMs是其重要组成部

分, 是微环境中浸润数目最多的免疫细胞, 与肿瘤血管生成和预后相关<sup>[6-8]</sup>. 研究表明, TAMs能促进多种肿瘤的发生和<sup>[9]</sup>. 巨噬细胞具有明显的可塑性, 在不同的微环境信号刺激下可改变自身形态和功能, 分化成不同的细胞群, 即巨噬细胞极化. 根据活化状态, 主要将其分为经典激活的巨噬细胞(classically activated macrophage, M1)和替代活化巨噬细胞(alternatively activated macrophage, M2). M1和M2型是巨噬细胞极化的两个极端类型, 二者可相互转化, 正常时处于动态平衡之中, 局部M1和M2型巨噬细胞的动态失衡将影响疾病的发生和发展<sup>[10-13]</sup>. 在肿瘤组织中能同时发现M1和M2型巨噬细胞, M1型巨噬细胞可杀伤肿瘤细胞, 抑制肿瘤血管和淋巴管生成. TAMs被认为是倾向于M2型分化特异的巨噬细胞, 恶性肿瘤初始和发展的标志之一就是巨噬细胞类型从M1型向M2型的极化<sup>[14,15]</sup>. 报道显示, 阻断TAMs和肿瘤细胞之间的相互作用、抑制巨噬细胞M2极化都可以防止肿瘤的发生和转移<sup>[16-19]</sup>. 因此, 巨噬细胞极化机制的研究有望为肿瘤的治疗提供新靶点.

## 2 长链非编码RNA及其调控巨噬细胞极化

人类基因组包含的大量核苷酸序列经过转录和翻译后转化为蛋白质, 然而仅有大约2%的RNA可以编码蛋白. 近年来发现剩余部分的RNA虽不编码蛋白质, 但在细胞生物学功能中发挥重要作用, 这部分RNA被称为非编码RNA (non-coding RNA, ncRNAs)<sup>[20]</sup>. 长度超过200个核苷酸的非编码RNA被称为lncRNAs, 其广泛存在于哺乳动物体内<sup>[21]</sup>. 根据lncRNAs在基因组上相对于蛋白质编码基因的位置, 可将其分为正义链(sense)、反义链(antisense)、双向链(bidirectional)、内含子间(intronic)和基因间(intergenic)五种, 也可根据在细胞中分布的位置分为核lncRNAs和细胞质lncRNAs, 并且可以根据各自的位置来推断其具有的功能<sup>[22,23]</sup>. lncRNAs通过与大量生物分子, 如RNA、DNA和蛋白质等相互作用, 对基因表达的转录、转录后表观遗传调控来影响基因表达, 参与细胞增殖、分化、凋亡等生命活动过程, 在恶性肿瘤基因表达中发挥着重要调控作用<sup>[24-28]</sup>. 研究发现lncRNA HIF1A-AS2<sup>[29]</sup>和lncRNA GAPLINC<sup>[30]</sup>在胃癌细胞系中过表达, lncRNAs的生物学功能和肿瘤的发生之间的关系已经得到证实<sup>[31]</sup>, 但是其具体的机制有待进一步的研究和阐释. 目前的研究发现lncRNAs在固有免疫中发挥重要的调控作用, 新近的一些研究提示lncRNAs调节巨噬细胞极化过程参与疾病进展<sup>[32,33]</sup>. lncRNAs表达谱分析有助于胃癌的诊断和预后判断, 可作为胃癌介入治疗的有效靶点.

以往针对lncRNAs的研究着眼于基因组印记、发育过程和癌症, 但是越来越多的证据指向lncRNAs在巨



噬细胞极化进程中发挥重要调控作用。例如, 腺癌转移相关转录本1 (long non-coding RNA metastasis-associated lung adenocarcinoma transcript 1, LncRNA MALAT1)抑制M1极化过程<sup>[34,35]</sup>; 巨噬细胞M2极化调制物(LncRNA MM2P)促进了M2的极化<sup>[36]</sup>, 乳腺癌脑转移蛋白(LncRNA BM)也参与了巨噬细胞的极化过程, 发挥促进M2极化的作用, 这些研究提示LncRNAs参与了肿瘤微环境中巨噬细胞极化的过程<sup>[37]</sup>。研究发现, LINC00240通过miR-124-3p/DNMT3B轴促进胃癌细胞增殖、迁移<sup>[38]</sup>。胃癌局部微环境中, lncRNAs通过调控转录因子, 进一步改变巨噬细胞极化方向。

尽管研究者一直致力于研究lncRNAs调控基因表达的机制, 但是在表征决定巨噬细胞M2极化的功能性lncRNAs方面的研究进展甚微。LINC00662促进M2极化过程在肝癌中发挥癌基因的作用, 其可能通过ceRNA机制竞争性结合miR-15a, miR-16、miR-107, 从而促进WNT3A的分泌, 同时其也通过旁分泌途径激活Wnt/ $\beta$ -catenin信号通路, 继而促进M2极化<sup>[39]</sup>。

### 3 lncRNAs和肿瘤相关

大量的研究证明lncRNAs与包括胃癌在内的诸多肿瘤的发生和发展有着密切的关联。例如Sang等<sup>[40]</sup>人筛选发现了LncRNA-CamK-A调控信号介导的肿瘤微环境的重塑, 这一报道表明了lncRNAs对肿瘤微环境中Ca<sup>2+</sup>依赖信号转导途径的重要性, 可能会为人类提供一个肿瘤免疫治疗的潜在靶点; Sun等<sup>[41]</sup>人报道了LncRNA GAS5抑制胶质小细胞M2极化, 加剧脱髓鞘, 因而GAS5有望成为治疗脱髓鞘疾病的一个靶点。此外还有Chen等<sup>[42]</sup>报道的LncRNA LNMAT1通过CCL2依赖型巨噬细胞募集促进膀胱癌淋巴转移, 以及Wang等<sup>[37]</sup>报道的JAK2结合长链非编码RNA促进乳腺癌脑转移。此外, 在卵巢癌<sup>[43]</sup>、肺癌<sup>[44]</sup>、食管癌<sup>[45]</sup>、甲状腺癌<sup>[46,47]</sup>、肝癌<sup>[48]</sup>等多种肿瘤的发生、发展中均观察到lncRNAs的身影。

吴昊<sup>[49]</sup>在人的胃癌组织和癌旁组织中分离出的M2型巨噬细胞中检测出LncRNA NR\_028高表达, 敲低其表达可以使肿瘤的转移和大小明显减弱, 表明其可能促进胃癌的进展, CHI3L1和ARG1蛋白可能参与这一相互作用的过程。Xie等<sup>[50]</sup>发现LncRNA ANCR过表达可下调<sup>[51]</sup>FoxO1抑制巨噬细胞向M1的极化, 促进胃癌细胞的侵袭和转移。Nie等<sup>[52]</sup>人发现一条新的LncRNA-miRNA-mRNA (H19-miR-29a-3p-COL1A2)轴可能参与巨噬细胞极化过程, 为胃癌的治疗提供新的策略。李燕等<sup>[53]</sup>人发现胃癌细胞的LncRNA Hotair能够被巨噬细胞摄取, 并且将其转化为癌症相关巨噬细胞, 表现出一定的促癌特性, 这为胃癌的治疗提供新的可能的靶点。此外, 黄自坤等<sup>[51]</sup>在小鼠RAW264.7巨噬细胞实验中发现LncRNA-

cox2参与调控极化过程, 为针对以M1极化为靶点的相关疾病诊治提供理论依据和实验依据。蒋莉等<sup>[54]</sup>人报道了LncRNA-MM2P可能通过转录因子STAT6的磷酸化水平来调控巨噬细胞极化, 干扰其表达可抑制肿瘤生长。但有趣的是沉默此lncRNA, 对M2型巨噬细胞促肿瘤细胞迁移能力无影响, 这提示通过靶向单一LncRNA来控制肿瘤的效果可能不是很好。越来越多的实验证据表明lncRNAs在调控胃癌巨噬细胞极化方面有着重要的作用。从目前所得的结果来看, 通过阻断肿瘤巨噬细胞极化过程来实现肿瘤的治疗是有希望的(图1)。尽管目前发现了一些lncRNAs调节胃癌巨噬细胞极化的过程, 但是完整的调节通路并没有揭示, 这有待解决(表1)。

此外, 关于lncRNAs在胃癌中的其他调节通路的研究也取得了诸多的进展。如Kong等<sup>[55]</sup>人报道了一种新的LncRNA ZFPM2-AS1通过稳定迁移抑制因子(migration inhibition factor, MIF)减弱p53通路(ZFPM2-AS1/MIF/p53轴), 促进癌症的发生。Li等<sup>[38]</sup>的报道表明LINC00240通过miR-124-3p/DNMT3B轴促进胃癌细胞增殖、迁移。喻大军等<sup>[56]</sup>的报道显示, LncRNA NEAT1在胃癌中可能通过调控miR-103a/STAMBPL1轴改变胃癌细胞增殖及侵袭能力。诸多的研究表明了lncRNAs在肿瘤发生和发展中的重要作用, 有望通过其作为靶点进行诊断和治疗。

### 4 长链非编码RNA在胃癌的临床应用

大多数胃癌患者发现时已经处于晚期, 失去了手术根治的机会, 放化疗、免疫治疗等方式疗效有限, 因此迫切需要寻找胃癌早期生物标志物。越来越多的证据表明, 胃癌患者血清标本lncRNAs表达谱不同于健康者。lncRNAs在血浆中以高度稳定的形式被检测到, 有作为胃癌早期肿瘤标志物的巨大潜力。Arita等<sup>[57]</sup>发现胃癌患者血浆H19水平高于正常、术后可降低<sup>[58]</sup>。血浆中lncRNAs FAM49B-AS、GUSBP11和CTDHUT组合也有很大潜力成为胃癌诊断无创性生物标志物<sup>[59,60]</sup>。此外, 肿瘤预后的预测和评估是肿瘤诊治中的另一个要点。CASC19高表达患者的生存率明显低于低表达者, CASC19被认为是进展期胃癌患者总生存率的独立预后因素<sup>[61]</sup>。lncRNA NEAT1的过表达程度与临床分期、组织学类型、远处转移或淋巴转移呈正相关。单因素和多因素分析均显示NEAT1的过表达是胃癌患者预后不良的独立因素<sup>[62]</sup>。循环中CASC19和lncRNA NEAT1均可能成为胃癌患者新的预后标志物。此外, 胃癌患者血清LncRNA CUDR 等的异常表达, 为使用lncRNAs作为胃癌潜在肿瘤标志物进行诊断和预后提供依据<sup>[63]</sup>。尽管近年来胃癌患者的5年生存率有所提升, 但是还未达到理想水平。因此, 筛选新的胃癌标记物用于早期诊断和干预对改善患者预后至关重要。此外, 胃癌中Hotair表达上



表 1 长链非编码RNA调节胃癌巨噬细胞极化

作者	LncRNA	因子	对M1/M2极化的影响	Ref.
吴昊	LncRNA NR_028	CHI3L1; ARG1	促进M2	49
Xie	LncRNA ANCR	FoxO1	抑制M1	50
Nie	LncRNA H19	miR-29a-3p; COL1A2	促进M1向M2	52
李燕	LncRNA Hotaic		促进M2	53
黄白坤	LncRNA-cox2		促进M1、抑制M2	51
蒋莉	LncRNA MM2P	STAT	促进M2	54

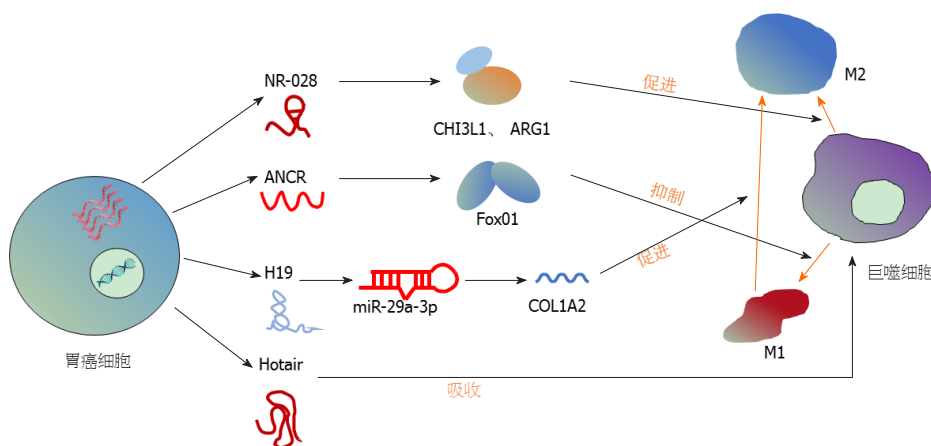


图 1 长链非编码RNA调控胃癌巨噬细胞极化路径。

调与肿瘤大小、晚期病理分期、转移和患者低生存率等相关,也可以作为患者预后不良的标志物<sup>[64,65]</sup>。因此lncRNAs在胃癌的诊断、治疗以及评估预后等方面的价值应当引起人们的注意。

## 5 展望

胃癌是一种异质性疾病,尽管幽门螺杆菌的控制显著改善了胃癌的发病现状,但是进展期和转移性胃癌的治疗现状仍不能令人满意。目前,许多新的治疗方式和新的诊治靶点的研究正在进行当中。肿瘤微环境对胃癌的异质性有一定作用,而作为微环境中主要的成分,TAMs的研究无疑是胃癌诊治的重点。现有的RT-PCR、LncRNA微阵列等LncRNA筛选技术的进步为相关研究提供了巨大的便利,但是临床需要更加简捷的技术来筛选相关的lncRNAs,以期对相关研究提供大容量的临床数据和更加有力的证据。尽管目前已有诸多研究着眼于胃癌和lncRNAs信号通路的研究,并且已有了大量的成果。但是对于lncRNAs调节胃癌巨噬细胞极化方面的研究不多,少量的结果也并未很好的揭示相关通路的全貌,离将其作为靶点进行治疗还有一定的距离,期待后期有更多的研究。下一步除了继续筛选可作为肿瘤标志物的单个或者组合lncRNA外,应该有相当一部分工作集中于筛选与M2型巨噬细胞极化相关的lncRNA,并且要回答其如何

影响巨噬细胞极化过程,从而寻求治疗靶点。并且从现有研究来看,多个lncRNA参与这一调控过程,寻找共同路径或各路径交集对相关的治疗研究有深远意义。相信lncRNAs相关的研究将能够为胃癌的精准化诊断、治疗提供新的靶点。

## 6 参考文献

- 1 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020; 70: 7-30 [PMID: 31912902 DOI: 10.3322/caac.21590]
- 2 本刊编辑部. 《中国肿瘤临床》文章荐读: 中国胃癌流行病学现状. *中国肿瘤临床* 2018; 45: 324
- 3 Wagner AD, Syn NL, Moehler M, Grothe W, Yong WP, Tai BC, Ho J, Unverzagt S. Chemotherapy for advanced gastric cancer. *Cochrane Database Syst Rev* 2017; 8: CD004064 [PMID: 28850174 DOI: 10.1002/14651858.CD004064.pub4]
- 4 慕芳, 武霞, 刘颖. 高表达CXCL12、IGF1胃癌组织临床病理特征及预后分析. *中华普外科手术学杂志(电子版)* 2018; 12: 306-308 [DOI: 10.3877/cma.jissn.1674-3946.2018.04.012]
- 5 Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? *Lancet* 2001; 357: 539-545 [PMID: 11229684 DOI: 10.1016/S0140-6736(00)04046-0]
- 6 Naora H. Heterotypic cellular interactions in the ovarian tumor microenvironment: biological significance and therapeutic implications. *Front Oncol* 2014; 4: 18 [PMID: 24567915 DOI: 10.3389/fonc.2014.00018]
- 7 Kim J, Bae JS. Tumor-Associated Macrophages and Neutrophils in Tumor Microenvironment. *Mediators Inflamm* 2016; 2016: 6058147 [PMID: 26966341 DOI: 10.1155/2016/6058147]
- 8 Chanmee T, Ontong P, Konno K, Itano N. Tumor-associated macrophages as major players in the tumor microenvironment. *Cancers (Basel)* 2014; 6: 1670-1690 [PMID: 25125485 DOI: 10.3390/

- cancers6031670]
- 9 Pollard JW. Tumour-educated macrophages promote tumour progression and metastasis. *Nat Rev Cancer* 2004; 4: 71-78 [PMID: 14708027 DOI: 10.1038/nrc1256]
- 10 Sica A, Erreni M, Allavena P, Porta C. Macrophage polarization in pathology. *Cell Mol Life Sci* 2015; 72: 4111-4126 [PMID: 26210152 DOI: 10.1007/s00018-015-1995-y]
- 11 黄自坤, 李俊明. 巨噬细胞极化及其在感染性疾病中的作用. *国际免疫学杂志* 2012; 35: 255-258+281 [DOI: 10.3760/cma.jissn.1673-4394.2012.04.003]
- 12 李小鹏, 张伦理. 巨噬细胞极化现象与结核病的关系. *中华微生物学和免疫学杂志* 2014; 34: 247-250 [DOI: 10.3760/cma.jissn.0254-5101.2014.03.018]
- 13 Yoon J, Um HN, Jang J, Bae YA, Park WJ, Kim HJ, Yoon MS, Chung IY, Jung Y. Eosinophil Activation by Toll-Like Receptor 4 Ligands Regulates Macrophage Polarization. *Front Cell Dev Biol* 2019; 7: 329 [PMID: 31921842 DOI: 10.3389/fcell.2019.00329]
- 14 Guo X, Zhao Y, Yan H, Yang Y, Shen S, Dai X, Ji X, Ji F, Gong XG, Li L, Bai X, Feng XH, Liang T, Ji J, Chen L, Wang H, Zhao B. Single tumor-initiating cells evade immune clearance by recruiting type II macrophages. *Genes Dev* 2017; 31: 247-259 [PMID: 28223311 DOI: 10.1101/gad.294348.116]
- 15 Mantovani A, Marchesi F, Malesci A, Laghi L, Allavena P. Tumour-associated macrophages as treatment targets in oncology. *Nat Rev Clin Oncol* 2017; 14: 399-416 [PMID: 28117416 DOI: 10.1038/nrclinonc.2016.217]
- 16 Zhou Q, Xian M, Xiang S, Xiang D, Shao X, Wang J, Cao J, Yang X, Yang B, Ying M, He Q. All-Trans Retinoic Acid Prevents Osteosarcoma Metastasis by Inhibiting M2 Polarization of Tumor-Associated Macrophages. *Cancer Immunol Res* 2017; 5: 547-559 [PMID: 28515123 DOI: 10.1158/2326-6066.CIR-16-0259]
- 17 Dong R, Gong Y, Meng W, Yuan M, Zhu H, Ying M, He Q, Cao J, Yang B. The involvement of M2 macrophage polarization inhibition in fenretinide-mediated chemopreventive effects on colon cancer. *Cancer Lett* 2017; 388: 43-53 [PMID: 27913199 DOI: 10.1016/j.canlet.2016.11.029]
- 18 Li X, Yao W, Yuan Y, Chen P, Li B, Li J, Chu R, Song H, Xie D, Jiang X, Wang H. Targeting of tumour-infiltrating macrophages via CCL2/CCR2 signalling as a therapeutic strategy against hepatocellular carcinoma. *Gut* 2017; 66: 157-167 [PMID: 26452628 DOI: 10.1136/gutjnl-2015-310514]
- 19 Sprinzl MF, Puschnik A, Schlitter AM, Schad A, Ackermann K, Esposito I, Lang H, Galle PR, Weinmann A, Heikenwälder M, Protzer U. Sorafenib inhibits macrophage-induced growth of hepatoma cells by interference with insulin-like growth factor-1 secretion. *J Hepatol* 2015; 62: 863-870 [PMID: 25463538 DOI: 10.1016/j.jhep.2014.11.011]
- 20 Evans JR, Feng FY, Chinnaiyan AM. The bright side of dark matter: lncRNAs in cancer. *J Clin Invest* 2016; 126: 2775-2782 [PMID: 27479746 DOI: 10.1172/JCI84421]
- 21 Bhan A, Soleimani M, Mandal SS. Long Noncoding RNA and Cancer: A New Paradigm. *Cancer Res* 2017; 77: 3965-3981 [PMID: 28701486 DOI: 10.1158/0008-5472.CAN-16-2634]
- 22 Rinn JL, Chang HY. Genome regulation by long noncoding RNAs. *Annu Rev Biochem* 2012; 81: 145-166 [PMID: 22663078 DOI: 10.1146/annurev-biochem-051410-092902]
- 23 St Laurent G, Wahlestedt C, Kapranov P. The Landscape of long noncoding RNA classification. *Trends Genet* 2015; 31: 239-251 [PMID: 25869999 DOI: 10.1016/j.tig.2015.03.007]
- 24 Lau E. Non-coding RNA: Zooming in on lncRNA functions. *Nat Rev Genet* 2014; 15: 574-575 [PMID: 25048169 DOI: 10.1038/nrg3795]
- 25 Yang ZG, Gao L, Guo XB, Shi YL. Roles of long non-coding RNAs in gastric cancer metastasis. *World J Gastroenterol* 2015; 21: 5220-5230 [PMID: 25954095 DOI: 10.3748/wjg.v21.i17.5220]
- 26 Sigova AA, Mullen AC, Molin B, Gupta S, Orlando DA, Guenther MG, Almada AE, Lin C, Sharp PA, Giallourakis CC, Young RA. Divergent transcription of long noncoding RNA/mRNA gene pairs in embryonic stem cells. *Proc Natl Acad Sci USA* 2013; 110: 2876-2881 [PMID: 23382218 DOI: 10.1073/pnas.1221904110]
- 27 Mathy NW, Chen XM. Long non-coding RNAs (lncRNAs) and their transcriptional control of inflammatory responses. *J Biol Chem* 2017; 292: 12375-12382 [PMID: 28615453 DOI: 10.1074/jbc.R116.760884]
- 28 Li LJ, Leng RX, Fan YG, Pan HF, Ye DQ. Translation of noncoding RNAs: Focus on lncRNAs, pri-miRNAs, and circRNAs. *Exp Cell Res* 2017; 361: 1-8 [PMID: 29031633 DOI: 10.1016/j.yexcr.2017.10.010]
- 29 Chen WM, Huang MD, Kong R, Xu TP, Zhang EB, Xia R, Sun M, De W, Shu YQ. Antisense Long Noncoding RNA HIF1A-AS2 Is Upregulated in Gastric Cancer and Associated with Poor Prognosis. *Dig Dis Sci* 2015; 60: 1655-1662 [PMID: 25686741 DOI: 10.1007/s10620-015-3524-0]
- 30 Yan X, Hu Z, Feng Y, Hu X, Yuan J, Zhao SD, Zhang Y, Yang L, Shan W, He Q, Fan L, Kandalaft LE, Tanyi JL, Li C, Yuan CX, Zhang D, Yuan H, Hua K, Lu Y, Katsaros D, Huang Q, Montone K, Fan Y, Coukos G, Boyd J, Sood AK, Rebbeck T, Mills GB, Dang CV, Zhang L. Comprehensive Genomic Characterization of Long Non-coding RNAs across Human Cancers. *Cancer Cell* 2015; 28: 529-540 [PMID: 26461095 DOI: 10.1016/j.ccell.2015.09.006]
- 31 Damas ND, Marcatti M, Côme C, Christensen LL, Nielsen MM, Baumgartner R, Gylling HM, Maglieri G, Rundsten CF, Seemann SE, Rapin N, Thézenas S, Vang S, Ørntoft T, Andersen CL, Pedersen JS, Lund AH. SNHG5 promotes colorectal cancer cell survival by counteracting STAU1-mediated mRNA destabilization. *Nat Commun* 2016; 7: 13875 [PMID: 28004750 DOI: 10.1038/ncomms13875]
- 32 Li L, Dang Q, Xie H, Yang Z, He D, Liang L, Song W, Yeh S, Chang C. Infiltrating mast cells enhance prostate cancer invasion via altering lncRNA-HOTAIR/PRC2-androgen receptor (AR)-MMP9 signals and increased stem/progenitor cell population. *Oncotarget* 2015; 6: 14179-14190 [PMID: 25895025 DOI: 10.18632/oncotarget.3651]
- 33 Zhang D, Ding L, Li Y, Ren J, Shi G, Wang Y, Zhao S, Ni Y, Hou Y. Midkine derived from cancer-associated fibroblasts promotes cisplatin-resistance via up-regulation of the expression of lncRNA ANRIL in tumour cells. *Sci Rep* 2017; 7: 16231 [PMID: 29176691 DOI: 10.1038/s41598-017-13431-y]
- 34 Cui H, Banerjee S, Guo S, Xie N, Ge J, Jiang D, Zörnig M, Thannickal VJ, Liu G. Long noncoding RNA Malat1 regulates differential activation of macrophages and response to lung injury. *JCI Insight* 2019; 4 [PMID: 30676324 DOI: 10.1172/jci.insight.124522]
- 35 Zhao G, Su Z, Song D, Mao Y, Mao X. The long noncoding RNA MALAT1 regulates the lipopolysaccharide-induced inflammatory response through its interaction with NF- $\kappa$ B. *FEBS Lett* 2016; 590: 2884-2895 [PMID: 27434861 DOI: 10.1002/1873-3468.12315]
- 36 Cao J, Dong R, Jiang L, Gong Y, Yuan M, You J, Meng W, Chen Z, Zhang N, Weng Q, Zhu H, He Q, Ying M, Yang B. lncRNA-MM2P Identified as a Modulator of Macrophage M2 Polarization. *Cancer Immunol Res* 2019; 7: 292-305 [PMID: 30459152 DOI: 10.1158/2326-6066.CIR-18-0145]
- 37 Wang S, Liang K, Hu Q, Li P, Song J, Yang Y, Yao J, Mangala LS, Li C, Yang W, Park PK, Hawke DH, Zhou J, Zhou Y, Xia W, Hung MC, Marks JR, Gallick GE, Lopez-Berestein G, Flores ER, Sood AK, Huang S, Yu D, Yang L, Lin C. JAK2-binding long noncoding RNA promotes breast cancer brain metastasis. *J Clin Invest* 2017; 127: 4498-4515 [PMID: 29130936 DOI: 10.1172/JCI91553]
- 38 Li Y, Yan J, Wang Y, Wang C, Zhang C, Li G. LINC00240 promotes gastric cancer cell proliferation, migration and EMT via the miR-124-3p / DNMT3B axis. *Cell Biochem Funct* 2020; 38: 1079-1088 [PMID: 32526811 DOI: 10.1002/cbf.3551]
- 39 Tian X, Wu Y, Yang Y, Wang J, Niu M, Gao S, Qin T, Bao D. Long noncoding RNA LINC00662 promotes M2 macrophage polarization and hepatocellular carcinoma progression via activating Wnt/ $\beta$ -catenin signaling. *Mol Oncol* 2020; 14: 462-483

- [PMID: 31785055 DOI: 10.1002/1878-0261.12606]
- 40 Sang LJ, Ju HQ, Liu GP, Tian T, Ma GL, Lu YX, Liu ZX, Pan RL, Li RH, Piao HL, Marks JR, Yang LJ, Yan Q, Wang W, Shao J, Zhou Y, Zhou T, Lin A. LncRNA CamK-A Regulates  $Ca^{2+}$ -Signaling-Mediated Tumor Microenvironment Remodeling. *Mol Cell* 2018; 72: 71-83.e7 [PMID: 30220561 DOI: 10.1016/j.molcel.2018.08.014]
  - 41 Sun D, Yu Z, Fang X, Liu M, Pu Y, Shao Q, Wang D, Zhao X, Huang A, Xiang Z, Zhao C, Franklin RJ, Cao L, He C. LncRNA GAS5 inhibits microglial M2 polarization and exacerbates demyelination. *EMBO Rep* 2017; 18: 1801-1816 [PMID: 28808113 DOI: 10.15252/embr.201643668]
  - 42 Chen C, He W, Huang J, Wang B, Li H, Cai Q, Su F, Bi J, Liu H, Zhang B, Jiang N, Zhong G, Zhao Y, Dong W, Lin T. LNMAT1 promotes lymphatic metastasis of bladder cancer via CCL2 dependent macrophage recruitment. *Nat Commun* 2018; 9: 3826 [PMID: 30237493 DOI: 10.1038/s41467-018-06152-x]
  - 43 Zeng XY, Xie H, Yuan J, Jiang XY, Yong JH, Zeng D, Dou YY, Xiao SS. M2-like tumor-associated macrophages-secreted EGF promotes epithelial ovarian cancer metastasis via activating EGFR-ERK signaling and suppressing lncRNA LIMT expression. *Cancer Biol Ther* 2019; 20: 956-966 [PMID: 31062668 DOI: 10.1080/15384047.2018.1564567]
  - 44 Sun Y, Xu J. TCF-4 Regulated lncRNA-XIST Promotes M2 Polarization Of Macrophages And Is Associated With Lung Cancer. *Onco Targets Ther* 2019; 12: 8055-8062 [PMID: 31632059 DOI: 10.2147/OTT.S210952]
  - 45 Liu Y, Wang L, Liu H, Li C, He J. The Prognostic Significance of Metabolic Syndrome and a Related Six-lncRNA Signature in Esophageal Squamous Cell Carcinoma. *Front Oncol* 2020; 10: 61 [PMID: 32133283 DOI: 10.3389/fonc.2020.00061]
  - 46 Li JH, Zhang SQ, Qiu XG, Zhang SJ, Zheng SH, Zhang DH. Long non-coding RNA NEAT1 promotes malignant progression of thyroid carcinoma by regulating miRNA-214. *Int J Oncol* 2017; 50: 708-716 [PMID: 28000845 DOI: 10.3892/ijo.2016.3803]
  - 47 Huang JK, Ma L, Song WH, Lu BY, Huang YB, Dong HM, Ma XK, Zhu ZZ, Zhou R. LncRNA-MALAT1 Promotes Angiogenesis of Thyroid Cancer by Modulating Tumor-Associated Macrophage FGF2 Protein Secretion. *J Cell Biochem* 2017; 118: 4821-4830 [PMID: 28543663 DOI: 10.1002/jcb.26153]
  - 48 Lin YH, Wu MH, Yeh CT, Lin KH. Long Non-Coding RNAs as Mediators of Tumor Microenvironment and Liver Cancer Cell Communication. *Int J Mol Sci* 2018; 19 [PMID: 30477236 DOI: 10.3390/ijms19123742]
  - 49 吴昊. LncRNA NR\_028在胃癌免疫微环境相关巨噬细胞极化中的作用及机制研究. 河北医科大学 2019
  - 50 Xie C, Guo Y, Lou S. LncRNA ANCR Promotes Invasion and Migration of Gastric Cancer by Regulating FoxO1 Expression to Inhibit Macrophage M1 Polarization. *Dig Dis Sci* 2020; 65: 2863-2872 [PMID: 31894487 DOI: 10.1007/s10620-019-06019-1]
  - 51 黄自坤, 姚芳苒, 罗清, 叶建青, 邓楨, 弼阳, 江红, 李俊明. lincRNA-cox2对小鼠RAW264.7巨噬细胞极化的影响. 中华微生物学和免疫学杂志 2016; 36: 881-886 [DOI: 10.3760/cma.j.issn.0254-5101.2016.12.001]
  - 52 Nie K, Zheng Z, Wen Y, Pan J, Liu Y, Jiang X, Yan Y, Jiang K, Liu P, Xu S, Liu F, Li P. A novel ceRNA axis involves in regulating immune infiltrates and macrophage polarization in gastric cancer. *Int Immunopharmacol* 2020; 87: 106845 [PMID: 32763781 DOI: 10.1016/j.intimp.2020.106845]
  - 53 李燕, 周雄坤, 刘静, 苟亚军. 长链非编码RNA Hotair通过调控巨噬细胞表型转换促进胃癌细胞增殖与侵袭. 中华细胞与干细胞杂志(电子版) 2019; 9: 23-28 [DOI: 10.3877/cma.j.issn.2095-1221.2019.01.005]
  - 54 蒋莉, 董蓉, 龚彦玲, 袁梦, 朱虹, 应美丹, 何俏军, 曹戟, 杨波. LncRNA-MM2P:特异性调控巨噬细胞M2型极化的长链非编码RNA. 2018年药理学前沿国际研讨会暨浙江省药理学学会浙江省药学会药理专业委员会学术年会 2018
  - 55 Kong F, Deng X, Kong X, Du Y, Li L, Zhu H, Wang Y, Xie D, Guha S, Li Z, Guan M, Xie K. ZFPM2-AS1, a novel lncRNA, attenuates the p53 pathway and promotes gastric carcinogenesis by stabilizing MIF. *Oncogene* 2018; 37: 5982-5996 [PMID: 29985481 DOI: 10.1038/s41388-018-0387-9]
  - 56 喻大军, 郭晨旭, 李靖, 朱超, 金鑫, 王庆康, 钱军. lncRNA NEAT1/miR-103a/STAMBPL1轴对胃癌细胞增殖和侵袭的调控作用. 山西医科大学学报 2020; 51: 883-887 [DOI: 10.13753/j.jissn.1007-6611.2020.09.001]
  - 57 Arita T, Ichikawa D, Konishi H, Komatsu S, Shiozaki A, Shoda K, Kawaguchi T, Hirajima S, Nagata H, Kubota T, Fujiwara H, Okamoto K, Otsuji E. Circulating long non-coding RNAs in plasma of patients with gastric cancer. *Anticancer Res* 2013; 33: 3185-3193 [PMID: 23898077]
  - 58 Yang Y, Shao Y, Zhu M, Li Q, Yang F, Lu X, Xu C, Xiao B, Sun Y, Guo J. Using gastric juice lncRNA-ABHD11-AS1 as a novel type of biomarker in the screening of gastric cancer. *Tumour Biol* 2016; 37: 1183-1188 [PMID: 26280398 DOI: 10.1007/s13277-015-3903-3]
  - 59 Zheng R, Liang J, Lu J, Li S, Zhang G, Wang X, Liu M, Wang W, Chu H, Tao G, Zhao Q, Wang M, Du M, Qiang F, Zhang Z. Genome-wide long non-coding RNAs identified a panel of novel plasma biomarkers for gastric cancer diagnosis. *Gastric Cancer* 2019; 22: 731-741 [PMID: 30603909 DOI: 10.1007/s10120-018-00915-7]
  - 60 Tan H, Zhang S, Zhang J, Zhu L, Chen Y, Yang H, Chen Y, An Y, Liu B. Long non-coding RNAs in gastric cancer: New emerging biological functions and therapeutic implications. *Theranostics* 2020; 10: 8880-8902 [PMID: 32754285 DOI: 10.7150/thno.47548]
  - 61 Wang WJ, Guo CA, Li R, Xu ZP, Yu JP, Ye Y, Zhao J, Wang J, Wang WA, Zhang A, Li HT, Wang C, Liu HB. Long non-coding RNA CASC19 is associated with the progression and prognosis of advanced gastric cancer. *Aging (Albany NY)* 2019; 11: 5829-5847 [PMID: 31422382 DOI: 10.18632/aging.102190]
  - 62 Fu JW, Kong Y, Sun X. Long noncoding RNA NEAT1 is an unfavorable prognostic factor and regulates migration and invasion in gastric cancer. *J Cancer Res Clin Oncol* 2016; 142: 1571-1579 [PMID: 27095450 DOI: 10.1007/s00432-016-2152-1]
  - 63 Dong L, Qi P, Xu MD, Ni SJ, Huang D, Xu QH, Weng WW, Tan C, Sheng WQ, Zhou XY, Du X. Circulating CUDR, LSINCT-5 and PTENP1 long noncoding RNAs in sera distinguish patients with gastric cancer from healthy controls. *Int J Cancer* 2015; 137: 1128-1135 [PMID: 25694351 DOI: 10.1002/ijc.29484]
  - 64 Xia T, Chen S, Jiang Z, Shao Y, Jiang X, Li P, Xiao B, Guo J. Long noncoding RNA FER1L4 suppresses cancer cell growth by acting as a competing endogenous RNA and regulating PTEN expression. *Sci Rep* 2015; 5: 13445 [PMID: 26306906 DOI: 10.1038/srep13445]
  - 65 Li L, Jia F, Bai P, Liang Y, Sun R, Yuan F, Zhang L, Gao L. Association between polymorphisms in long non-coding RNA PRNCR1 in 8q24 and risk of gastric cancer. *Tumour Biol* 2016; 37: 299-303 [PMID: 26206497 DOI: 10.1007/s13277-015-3750-2]

科学编辑: 刘继红 制作编辑: 张砚梁







Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton,  
CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](https://www.wjgnet.com)



ISSN 1009-3079

