

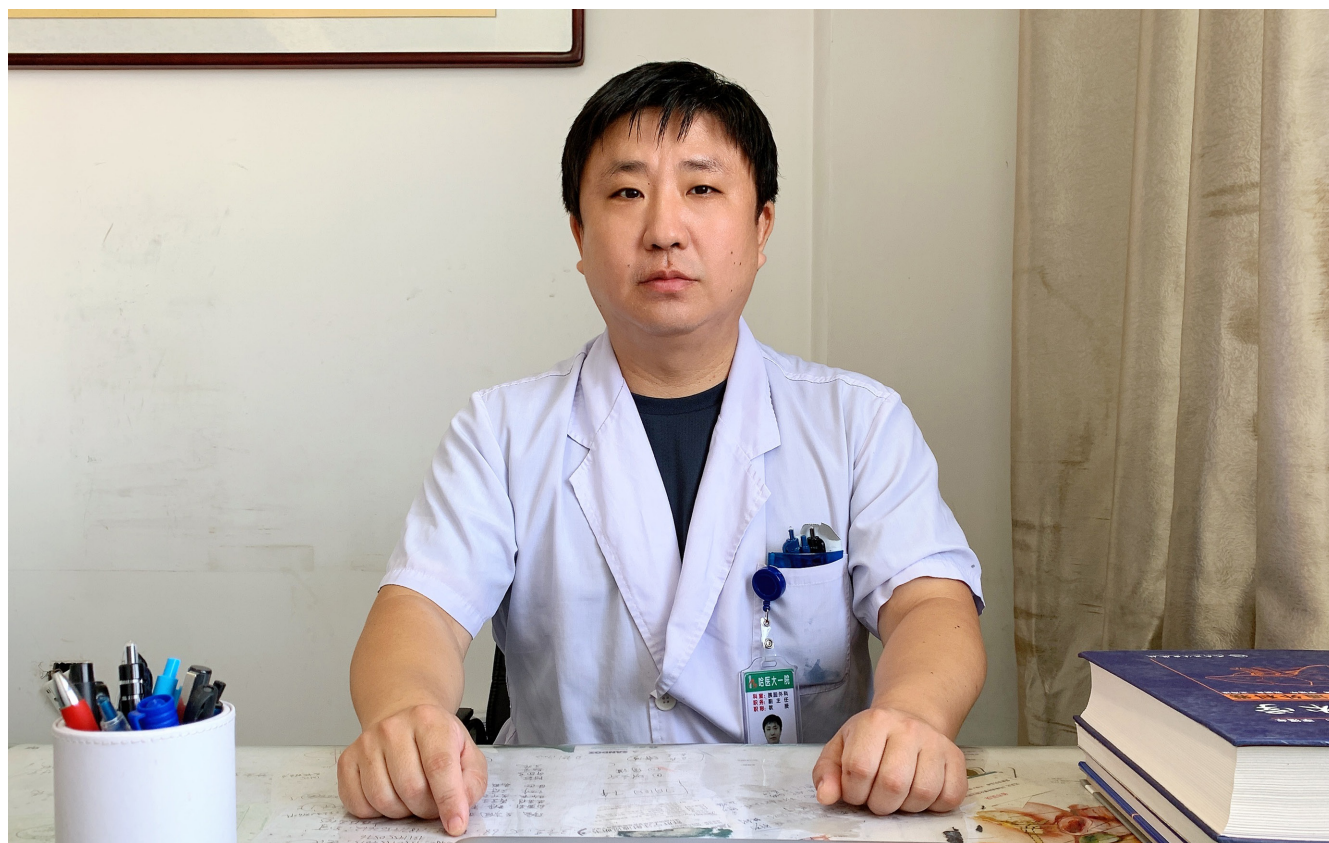
ISSN 1009-3079 (print)
ISSN 2219-2859 (online)

世界华人消化杂志®

WORLD CHINESE JOURNAL OF DIGESTOLOGY

Shijie Huaren Xiaohua Zazhi

2021 年 11 月 28 日 第 29 卷 第 22 期 (Volume 29 Number 22)



22 / 2021

ISSN 1009-3079



《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。



述评

- 1269 肠道菌群与胰腺炎: 现状及未来

温华, 李茜, 路宁, 苏媛媛, 马培晗, 张明鑫

基础研究

- 1276 circ_0000212靶向miR-139-5p对肝癌细胞增殖、迁移、侵袭、凋亡以及紫杉醇敏感性的影响

张惠忠, 张晓东, 黄建新

临床研究

- 1286 80岁及以上高龄患者原始乳头治疗性内镜逆行胰胆管造影术的临床分析

倪志, 张荣春, 潘阳林

- 1292 乳酸钠林格液和生理盐水治疗急性胰腺炎的荟萃分析

谷优优, 王珏磊, 陈宗南, 王肃, 刘晓智

文献综述

- 1298 减肥手术对反流性食管炎影响的研究进展

魏金平, 崔宏力

- 1304 结肠镜腺瘤检出率的近期研究进展

朱晓佳, 杨力

- 1311 生物制剂时代炎症性肠病的外科治疗

刘威, 周伟

临床实践

- 1316 叙事护理模式对进展期胰腺炎并发糖尿病患者自我管理能力和生活质量的影响

冯小华, 沈胜娟, 金根娟

消 息

- 1275 《世界华人消化杂志》参考文献要求
1285 《世界华人消化杂志》2011年开始不再收取审稿费
1303 《腹痛的诊断、鉴别诊断与治疗》书讯
1310 《世界华人消化杂志》性质、刊登内容及目标
1322 《世界华人消化杂志》正文要求

封面故事

王刚, 主任医师、教授、博士生导师, 哈尔滨医科大学附属第一医院肝胆外科病房副主任. 现任《中国研究型医院学会胰腺疾病专业委员会青委会》副主任委员、《黑龙江省医学会胰腺外科分会青委会》副主任委员等30余项学术兼职. 现已发表学术论文145篇, 第一作者及通讯作者92篇, 其中SCI收录文章36篇, 第一及通讯作者25篇, 单篇最高影响因子8.71, 单篇最高他引次数181次. 作为项目负责人, 主持国家自然科学基金4项、中国博士后基金1项、中国研究型医院学会消化道肿瘤专业委员会“晨星计划”基金1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 马玉洁; 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 2021-11-28

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<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<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.

Contents

Volume 29 Number 22 November 28, 2021

EDITORIAL

- 1269 Intestinal flora and pancreatitis: Present and future

Wen H, Li Q, Lu N, Su YY, Ma PH, Zhang MX

BASIC RESEARCH

- 1276 Circ_0000212 affects proliferation, migration, invasion, apoptosis, and paclitaxel sensitivity of liver cancer cells by targeting miR-139-5p

Zhang HZ, Zhang XD, Huang JX

CLINICAL RESEARCH

- 1286 Safety and efficacy of therapeutic endoscopic retrograde cholangiopancreatography in elderly patients with a native papilla

Ni Z, Zhang RC, Pan YL

- 1292 Meta-analysis of lactated Ringer's solution and normal saline for management of acute pancreatitis

Gu YY, Wang JL, Chen ZN, Wang S, Liu XZ

REVIEW

- 1298 Progress in understanding of influence of bariatric surgery on reflux esophagitis

Wei JP, Cui HL

- 1304 Progress in understanding of factors related to colonoscopic adenoma detection rate

Zhu XJ, Yang L

- 1311 Surgery for inflammatory bowel disease in the era of biologics

Liu W, Zhou W

CLINICAL PRACTICE

- 1316 Effect of narrative nursing model on self-management ability and quality of life of patients with advanced pancreatitis and diabetes

Feng XH, Shen SJ, Jin GJ

Contents

World Chinese Journal of Digestology
Volume 29 Number 22 November 28, 2021

COVER

Editorial Board Member of *World Chinese Journal of Digestology*, Gang Wang, Chief Physician, Professor, Doctoral Supervisor, Department of Pancreatic and Biliary Surgery, The First Affiliated Hospital of Harbin Medical University, No. 23 Youzheng Street, Nangang District, Harbin 150001, Heilongjiang Province, China. wjlu79@163.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: *Yu-Jie Ma* Layout Reviewer: *Lian-Sheng Ma*

Shijie Huaren Xiaohua Zazhi

Founded on January 15, 1993

Renamed on January 25, 1998

Publication date November 28, 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

<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

<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.

肠道菌群与胰腺炎: 现状及未来

温 华, 李 茜, 路 宁, 苏媛媛, 马培晗, 张明鑫

温华, 苏媛媛, 西安医学院 陕西省西安市 710000

温华, 李茜, 路宁, 苏媛媛, 张明鑫, 西安医学院第一附属医院消化内科 陕西省西安市 710077

马培晗, 张明鑫, 陕西中医药大学第二临床医学院 陕西省咸阳市 712046

温华, 主要从事肠道菌群与消化道疾病的研究。

基金项目: 陕西省教育厅专项项目, No.19JK0765; 陕西省自然科学基金基础研究计划一般项目(面上), No.2018JM7090。

作者贡献分布: 温华、李茜、路宁、苏媛媛及马培晗主要负责文献的收集与初稿的撰写; 温华及李茜负责文献的系统分析; 温华与路宁负责文章图表的制作; 张明鑫负责文稿的审校。

通讯作者: 张明鑫, 副主任医师, 博士, 710077, 西安市莲湖区丰镐西路48号, 西安医学院第一附属医院消化内科。zmx3115@163.com

收稿日期: 2021-07-30

修回日期: 2021-08-28

接受日期: 2021-10-08

在线出版日期: 2021-11-28

Intestinal flora and pancreatitis: Present and future

Hua Wen, Qian Li, Ning Lu, Yuan-Yuan Su, Pei-Han Ma, Ming-Xin Zhang

Hua Wen, Yuan-Yuan Su, Xi'an Medical University, Xi'an 710000, Shaanxi Province, China

Hua Wen, Qian Li, Ning Lu, Yuan-Yuan Su, Department of Gastroenterology, The First Affiliated Hospital of Xi'an Medical University, Xi'an 710077, Shaanxi Province, China

Pei-Han Ma, Ming-Xin Zhang, The Second Clinical Medical College, Shaanxi University of Traditional Chinese Medicine, Xianyang 712046, Shaanxi Province, China

Supported by: Special Project of Education Department of Shaanxi Province, No. 19JK0765; Natural Science Basic Research Program of Shaanxi Province, No. 2018JM7090.

Corresponding author: Ming-Xin Zhang, Associate Chief

Physician, Department of Gastroenterology, The First Affiliated Hospital of Xi'an Medical University, No. 48 Fenghao West Road, Xi'an 710077, Shaanxi Province, China. zmx3115@163.com

Received: 2021-07-30

Revised: 2021-08-28

Accepted: 2021-10-08

Published online: 2021-11-28

Abstract

The role of intestinal flora in human health and diseases has attracted more and more attention. At present, there have been some reports on the relationship between intestinal flora and pancreatitis. These reports reveal that intestinal flora plays some important roles in the occurrence and development of pancreatitis. The specific mechanisms of action are unclear, but there is a preliminary consensus that intestinal microbiome dysregulation promotes inflammatory changes in the pancreas. This paper summarizes the correlation between intestinal flora and pancreatitis, in order to provide some references and ideas for further research.

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

Key Words: Gut microbiota; Acute pancreatitis; Chronic pancreatitis; Autoimmune pancreatitis

Citation: Wen H, Li Q, Lu N, Su YY, Ma PH, Zhang MX. Intestinal flora and pancreatitis: Present and future. Shijie Huaren Xiaohua Zazhi 2021; 29(22): 1269-1275

URL: <https://www.wjgnet.com/1009-3079/full/v29/i22/1269.htm>

DOI: <https://dx.doi.org/10.11569/wcjd.v29.i22.1269>

摘要

肠道菌群在人类健康和疾病中的作用逐渐被人们重视。目前已有一些关于肠道菌群与胰腺炎关系的研究报道, 这些报道揭示了肠道菌群在胰腺炎发生发展过程中发挥着某些重要作用。目前还不清楚这些具体作

用机制, 但肠道菌群失调被认为促进胰腺炎症变化的假说已经有了初步的共识. 本文概述了肠道菌群与胰腺炎的相关性, 旨在为今后的进一步研究提供某些参考思路.

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

关键词: 肠道菌群; 急性胰腺炎; 慢性胰腺炎; 自身免疫性胰腺炎

核心提要: 肠道的微生物丰富, 物种多样性高, 肠道菌群与疾病密不可分. 菌群与胰腺炎也不例外, 它们之间存在着一个生物交互系统, 即菌群-肠道-胰腺轴. 肠道细菌通过“肠漏”、影响胰腺外分泌、分子交叉或模拟等机制来促进胰腺炎症的发生. 益生菌及其相关微生物制剂的使用可以改善胰腺炎症程度及减轻症状.

文献来源: 温华, 李茜, 路宁, 苏媛媛, 马培晗, 张明鑫. 肠道菌群与胰腺炎: 现状及未来. 世界华人消化杂志 2021; 29(22): 1269–1275

URL: <https://www.wjgnet.com/1009-3079/full/v29/i22/1269.htm>

DOI: <https://dx.doi.org/10.11569/wjcd.v29.i22.1269>

0 引言

健康人肠道菌群的特点是微生物丰富, 物种多样性高. 有人把肠道菌群称作“第二基因组”. 据报道人类肠道菌群包含 10^{13} - 10^{14} 个微生物, 以及超过 5×10^6 个决定了肠道菌群的基因^[1,2]. 在这种微环境中, 细菌为优势菌, 分为有害菌、中性菌及有益菌. 其中厚壁菌门和拟杆菌门是主要的细菌门, 占微生物总数的85%-90%, 而放线菌门和变形菌门数量较少, 最多占10%^[3](表1). 一般情况下, 中性菌及有益菌种类比有害细菌种类多. 但是, 当肠道微生态被打乱时, 有害细菌就会增多, 一些菌群生理功能就会相应丧失^[4,5]. 在这种不良环境中, 肠细胞之间的紧密连接减少, 导致粘膜屏障完整性的功能受损; 这种被称为“肠漏”的变化有时会导致细菌移位(图1), 并在胃肠道和全身性疾病的发展中起着关键作用^[6]. 近年来, 人们逐渐意识到肠道菌群在人类健康和疾病中起着重要的作用, 如炎症性肠病、肠易激综合征、阿尔茨海默病和糖尿病等疾病均跟肠道菌群有关^[1-10]. 同理, 肠道菌群对胰腺炎也有着重要的作用及影响^[11], 研究者们相信肠道菌群与胰腺之间存在着一个生物交互系统, 即“菌群-肠道-胰腺轴”^[12]. 本文就肠道菌群与胰腺炎的相互影响, 做了相关论述, 希望能为这方面的研究者提供一些借鉴和思考.

1 肠道菌群与急性胰腺炎

急性胰腺炎(acute pancreatitis, AP)是腺泡内胰蛋白酶原

和其他蛋白水解酶过早激活的结果, 导致胰腺腺泡损伤、炎症介质上调、细胞因子释放、全身炎症反应和微循环损伤^[13], 多跟暴饮暴食、胆石症、酒精、高脂血症、高钙血症及家族遗传史等这些因素有关. 多项研究表明肠道菌群跟AP也密切相关.

1.1 肠道菌群与AP密切相关 Zhang等^[14]研究显示AP患者的样本含有更多的拟杆菌和变形杆菌, 而厚壁菌和放线菌较少(表1). 既往研究也发现AP患者肠球菌、肠杆菌等潜在致病菌含量显著高于非感染组, 而双歧杆菌等益生菌含量显著低于非感染组; 由此可见, 肠道菌群失衡可能是导致AP易位感染的重要原因. 尽管细菌可能不是胰腺炎的诱因, 但炎症环境可能使这些微生物进入胰腺, 并使局部和全身炎症状况恶化. 有研究表明AP患者的淋巴结样本、浆膜标本、血液标本中可以培养出细菌, 这些细菌大多来自下消化道, 其中最常见的微生物是大肠杆菌(54%)^[15].

AP改变肠道菌群的机制可能是炎症导致肠屏障功能受损^[16](图1), 从而增加了肠道的通透性. 这可能是通过降低claudin 2/4的表达改变肠道的紧密连接来实现的^[17]. 器官衰竭和更大程度坏死的AP患者中具有较多的致病菌群^[18,19]. Tsiotos等^[20,21]研究也显示约30%胰腺坏死的无菌病例, 最终会被感染致病菌群, 而且具有更高的致死率(20%-30%). 这些研究都为“肠漏”机制提供了证据.

1.2 胰腺分泌抗菌肽可以抑制肠道菌群 抗微生物肽(CRAMP)是一种通过细菌膜具有抗微生物活性的蛋白质^[22,23]. 这种胰腺分泌的抗菌肽可以抑制肠道菌群(图1)^[24,25]. Orai1是胰腺抗菌肽胞吐所需的 Ca^{2+} 通道, 在AP发展过程中, 由于胰腺腺泡损伤或者Orai1通道的破坏导致胰腺分泌抗菌肽减少, 可能使肠道菌群失调, 有害菌群大量繁殖. 而有害菌群的增多又可能通过“肠漏”及炎症等机制反过来加重胰腺炎.

1.3 改变AP相关肠道菌群, 有望改善疾病预后 日本相关指南认为急性重症胰腺炎(severe acute pancreatitis, SAP)及胰腺坏死应早期使用抗菌药物. 其依据来自一项临床研究, 该研究结果显示预防用药组显著降低了死亡率及胰腺感染性坏死发生率^[26]. 有研究认为乳酸杆菌和双歧杆菌等益生菌可能有助于维持肠道屏障功能, 限制致病菌群的生长^[27,28]. 也有研究发现高负荷益生菌混合物可能对治疗有害^[29]. 由于目前益生菌对SAP患者的影响存在较大争议, 故还需要进一步的研究予以证明.

2 肠道菌群与慢性胰腺炎

慢性胰腺炎(chronic pancreatitis, CP)是一种以胰腺腺泡、导管和胰岛细胞持续性破坏及进行性纤维化为主要特征的慢性炎症性疾病, 因为胰腺结构的破坏从而导致外分泌和内分泌功能受损^[30,31]. 临床表现主要有腹痛、胰

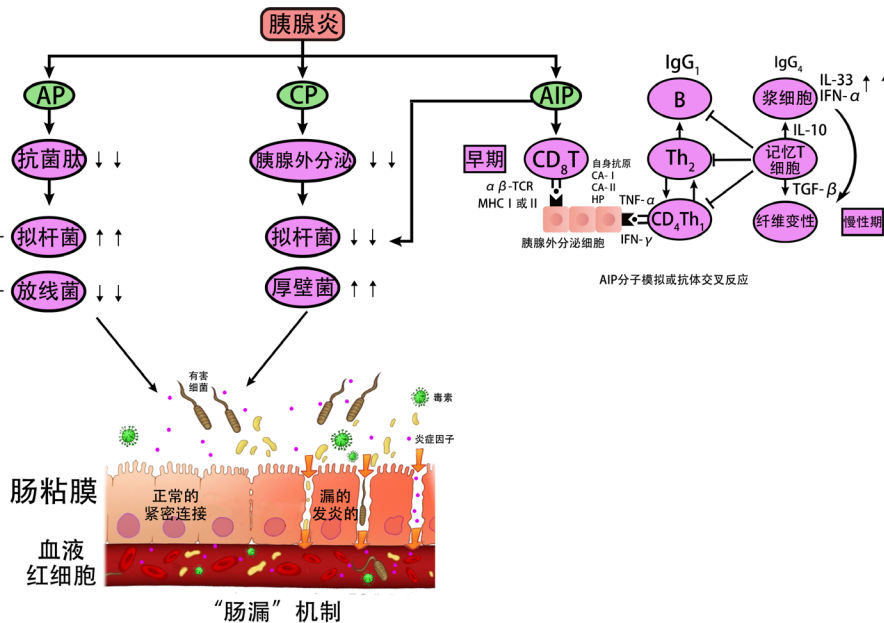


图1 肠道菌群与胰腺炎的相关机制. AP使胰腺腺泡损伤或者Orai1通道的破坏导致胰腺分泌抗菌肽减少, 从而使肠道变形菌和拟杆菌增加, 厚壁菌和放线菌减少, 有害菌的增多又可能导致肠道屏障受损从而形成“肠漏”. CP和AIP主要通过影响胰腺外分泌功能, 从而改变肠道菌群的种类和数量, 在有害菌和炎症的刺激下使肠道屏障受损形成“肠漏”. 在AIP早期, 对自身抗原或分子拟态(*H. pylori*)的初始反应是通过减少CD₈T细胞, 诱导产生IFN- γ 、TNF- α 等炎症因子, 补体系统的经典通路可能被IgG免疫复合物激活, 从而通过浆细胞样树突状细胞产生IFN- α 和IL-33, 最终介导慢性纤维炎症反应. AP: 急性胰腺炎; CP: 慢性胰腺炎; AIP: 自身免疫性胰腺炎; *H. pylori*: 幽门螺杆菌.

腺外分泌功能不全和高血糖等, 严重影响生活质量^[32], 同时CP患者也表现出与病原菌生长相关的生物失调^[33].

2.1 肠道菌群与CP的相互作用 和AP一样, 肠道菌群与CP也存在着相互影响. 有研究指出CP患者肠道菌群中拟杆菌的相对丰度显著增加, 厚壁菌的相对丰度降低^[34]. CP通过影响胰腺外分泌功能, 从而可以改变肠道菌群的种类和数量^[35]. 肠道菌群的改变可以使肠道屏障功能受损及通透性增加, 进而促使肠道菌群移位至胰腺, 进一步加重CP^[36-38](图1). 目前肠道菌群具体通过什么途径进入胰腺还不清楚, 需要进一步的研究.

2.2 胰酶替代疗法可以改善CP患者的肠道菌群 胰酶替代疗法(pancreatic enzyme replacement therapy, PERT)是胰腺外分泌不足(pancreatic exocrine insufficiency, PEI)治疗的基石. 通常认为粪便排泄异常, 脂肪泻和体重减轻的患者是PERT的适用人群, PERT可以帮助CP患者脂肪吸收, 改善患者的营养状况^[39]. 一些研究认为PERT可以直接改变肠道菌群, 但具体机制目前仍不清楚. 有研究发现用PERT治疗的小鼠中有相对丰富的阿克曼菌(*Akkermansia muciniphila*)和罗伊拉杆菌(*Latobacillus reuteri*). 特别是阿克曼菌, 在PERT组中发现高达58倍, 它可以通过促进粘液厚度和紧密连接蛋白表达来增强肠屏障功能, 从而减少“肠漏”^[40,41]. 综上, PERT可能有助于改善肠道菌群, 从而缓解CP患者症状.

2.3 微生物制剂可能改善CP患者的临床症状 Dos

Santos等^[42]发现使用由干酪乳杆菌、鼠李糖乳杆菌、嗜酸乳杆菌、双歧杆菌和果寡糖组成的合生元能改变CP患者的肠道微环境, 从而改善CP患者的临床和实验室结果. Dylag等^[43]也认为益生元可以使双歧杆菌增多, 致病菌减少, 从而维持肠道微生态^[44]. 这提示微生物制剂可能是一种治疗选择, 但其临床相关性还需要更多的研究支持.

3 肠道菌群与自身免疫性胰腺炎

自身免疫性胰腺炎(autoimmune pancreatitis, AIP)是一种特殊类型的胰腺炎, 常以梗阻性黄疸或腹痛为主要症状, 且伴有胰腺组织淋巴浆细胞浸润及纤维化, 治疗上对类固醇激素敏感^[45,46]. 它有两种不同的表型, 分为1型和2型. 目前, 1型AIP被认为是系统性免疫球蛋白G4相关疾病(IgG4-RD)的胰腺表现^[47], 它与血清IgG4浓度升高、淋巴浆细胞浸润和胰腺静脉炎有关. 与1型AIP不同, 2型AIP只影响胰腺, 血清IgG4浓度正常, 组织学上表现为中性粒细胞炎症^[48]. 有研究指出AIP和CP的肠道菌群在门类水平上无明显差异, 但是卵形拟杆菌、芦苇链球菌、戈登链球菌、乳酸发酵梭菌、拉瓦尔梭菌在CP患者中较AIP患者更常见^[49](表1).

3.1 肠道菌群可能与AIP相关 近期有人研究了幽门螺杆菌(*Helicobacter pylori*, *H. pylori*)感染与AIP之间的可能联系^[50-53]. Guarneri等^[53]提出*H. pylori*感染可能通过分子模拟

表 1 胰腺炎患者肠道菌群的变化

疾病谱	菌群变化	参考文献
健康者	厚壁菌门和拟杆菌门占85%–90%，放线菌门和变形菌门占10%.	[3]
急性胰腺炎患者	拟杆菌门和变形菌门的相对丰度显著增加，厚壁菌门和变形菌门的相对丰度显著降低.	[14]
慢性胰腺炎患者	拟杆菌门的相对丰度显著增加，厚壁菌门的相对丰度降低.	[34]
自身免疫性胰腺炎患者	在门水平上，自身免疫性胰腺炎和慢性胰腺炎患者之间没有差异. 然而，有些菌种比如卵形拟杆菌、产 芽链球菌、戈登链球菌、乳酸发酵梭菌、拉瓦尔梭菌在慢性胰腺炎患者中更常见.	[5]

表 2 肠道菌群与胰腺炎关系的研究

参考文献	研究类型	方法	疾病	结果	结论
[27]	前瞻性随机对照试验	45例AP患者: 22例植物乳杆菌 299(LP299) 活菌, 23例热杀灭LP299; 各 治疗1周	AP	治疗组感染性胰腺炎1/22例, 对照 组7/23例($P = 0.023$)	补充活LP299可以减少 手术治疗和胰腺相关脓 毒症的次数
[28]	前瞻性随机对照试验	74例AP患者中, 36例给予植物乳杆菌肠 内喂养, 38例给予肠外营养	AP	肠内营养组38.9%的患者被多种 微生物定植, 肠外营养组73.7% ($P < 0.01$); 肠内营养组30.6%的患者 被潜在致病菌定植, 肠外营养组为 50% ($P < 0.05$)	经肠内喂养可降低疾病 严重程度, 并有较好的 临床效果
[40]	前瞻性随机对照试验	对照组给予自来水. 胰酶处理组用胰淀 粉酶、脂肪酶和蛋白酶的混合物处理	CP	经胰酶处理的小鼠的细菌组成与对 照组有显著差异. AKK菌是肠道中的 一种关键的有益细菌, 在胰酶处理的 样本中显示出更高的相对丰度	PERT诱导有益细菌的 定植, 从而有助于减少 PEI相关症状, 并改善营 养状态
[42]	前瞻性随机对照试验	60例慢性胰腺炎患者: 干预组给予联合 用药, 对照组给予麦芽糊精12g/d	CP	治疗组大便次数明显减少: 治疗前平均 每天次数: 2.33($P < 0.153$); 治疗2月: 1.47 ($P = 0.002$); 治疗3月: 1.37 ($P =$ 0.012); 对照组大便次数无变化($P =$ 0.157)	益生元改善了CP患者 的临床和实验室结果, 这提示合生剂可能是一 种治疗选择
[50]	前瞻性随机对照试验	从20例自身免疫性胰腺炎患者中筛选免 疫球蛋白混合肽库. 从患者血清标本中 检测肽特异性抗体	AIP	18/20例血清标本识别出肽AIP(1– 7). 该肽与幽门螺杆菌PBP的氨基酸 序列和胰腺腺泡细胞中高表达的泛 素–蛋白连接酶E3组分n–识别蛋白 2(UBR2)同源	在大多数自身免疫性胰 腺炎患者中检测出特异 性抗体
[57]	前瞻性随机对照试验	我们研究了反复给药100 g聚肌苷–胞苷 酸(poly (I:C))对MRL/MpJ小鼠实验性AIP 诱导的肠道菌群先天免疫的作用	AIP	广泛使用抗生素的肠道灭菌可以抑 制产生IFN–和IL–33的pDCs的胰腺 积累, 从而抑制AIP的发展	肠道失调通过激活产生 IFN–和IL–33的pDCs增 加小鼠对实验性AIP的 敏感性

AP: 急性胰腺炎; CP: 慢性胰腺炎; AIP: 自身免疫性胰腺炎.

或抗体交叉反应在遗传个体中引发AIP(图1). Frulloni等^[50]研究表明*H. pylori*的α-碳酸酐酶(α-CA)与人类的α-碳酸酐酶-II (α-CA-II)以及*H. pylori*的纤溶酶原结合蛋白(PBP)与胰腺腺泡上皮细胞的泛素蛋白连接酶E3-n识别蛋白2存在一定同源性, 同区段含有DRB1*0405的结合序, 大多数AIP患者也表现出IgG反应活性. 同时, 95%的AIP患者血清抗体PBP阳性, 这提示*H. pylori*与胰腺自身蛋白的分子拟态可能是AIP发病的刺激因子. 所以, *H. pylori*感

染易感人群后可能会通过分子模拟诱发异常的免疫应答, 造成严重的组织损伤, 导致AIP发病.

3.2 肠道菌群的先天免疫反应参与了AIP的发展 先天免疫激活有助于AIP和IG4相关性疾病(IG4-RD)的发生发展^[54-56]. IG4-RD的特点是浆细胞样树突状细胞(pDCs)产生IFN-α和IL-33, 从而介导慢性纤维炎症反应. 有研究发现肠道菌群失调可以通过激活pDCs, 从而增加对AIP的敏感性; 另外, 使用广谱抗生素可以抑制胰腺产

生IFN- α 和IL-33介导的血小板聚集, 从而抑制AIP的发展^[57].

4 未来展望

近年来已有一些关于肠道菌群与胰腺炎关系的研究报道(表2). 肠道有益菌群可以通过维持肠道完整性和调节肠道屏障通透性可以抵御病原微生物, 所以理论上菌群的调节可能有助于胰腺炎和相关并发症的治疗. 但目前SAP患者是否应该使用益生菌治疗尚未达成共识. 益生菌可能对于改善SAP的肠黏膜屏障有一定作用, 但尚需进一步临床评价^[58]. 另外, 不同菌株的表现也不尽相同, 因为不同的细菌有不同的粘附位点和不同的免疫效果^[59,60]. 因此, 益生菌的种类可能导致临床结果的差异. 比如Cui等^[61]发现类似于双歧杆菌的益生菌可以显著改善感染程度及减轻症状. 而Gou等^[62]认为益生菌对预测SAP患者的临床结局既无益处也无副作用; 他们的研究还发现在益生菌的类型、剂量和治疗时间方面存在显著的异质性, 这可能导致了临床结局的异质性.

目前在不同研究中使用的益生菌类型和治疗策略还有较大差异, 所以在进行临床试验之前, 应考虑益生菌及其制剂的适当剂量和治疗时间. 另外, 考虑到一些益生菌的风险, 进一步的临床试验应该仔细设计, 以避免任何潜在的有害影响. 同时, 对胰腺炎相关菌群检测技术的选择及升级也很重要, 菌群检测常见的方法有细菌培养、聚合酶链式反应技术(PCR)、基于PCR基础上的16SrRNA技术、荧光原位杂交、基因芯片、宏基因组测序以及单一菌株或者人体完整菌群的移植、用免疫系统确认致病原因、用机器学习等高级算法整合多组学数据等, 有时候选择合适的检测技术及方法, 往往能达到事半功倍的效果. 当然, 菌群特异性改变的分析还可以利用易于收集的样本, 如根据血液、唾液和粪便等来开发出用于相应检测的新工具.

5 参考文献

- Marchesi JR, Adams DH, Fava F, Hermes GD, Hirschfield GM, Hold G, Quraishi MN, Kinross J, Smidt H, Tuohy KM, Thomas LV, Zoetendal EG, Hart A. The gut microbiota and host health: a new clinical frontier. *Gut* 2016; 65: 330-339 [PMID: 26338727 DOI: 10.1136/gutjnl-2015-309990]
- Thaiss CA, Zmora N, Levy M, Elinav E. The microbiome and innate immunity. *Nature* 2016; 535: 65-74 [PMID: 27383981 DOI: 10.1038/nature18847]
- Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiaro GAD, Gasbarrini A, Mele MC. What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. *Microorganisms* 2019; 7 [PMID: 30634578 DOI: 10.3390/microorganisms7010014]
- Zhang YJ, Li S, Gan RY, Zhou T, Xu DP, Li HB. Impacts of gut bacteria on human health and diseases. *Int J Mol Sci* 2015; 16: 7493-7519 [PMID: 25849657 DOI: 10.3390/ijms16047493]
- Forbes JD, Van Domselaar G, Bernstein CN. The Gut Microbiota in Immune-Mediated Inflammatory Diseases. *Front Microbiol* 2016; 7: 1081 [PMID: 27462309 DOI: 10.3389/fmicb.2016.01081]
- Camilleri M. Leaky gut: mechanisms, measurement and clinical implications in humans. *Gut* 2019; 68: 1516-1526 [PMID: 31076401 DOI: 10.1136/gutjnl-2019-318427]
- Agahi A, Hamidi GA, Daneshvar R, Hamdieh M, Soheili M, Alinaghpour A, Esmaeili Taba SM, Salami M. Does Severity of Alzheimer's Disease Contribute to Its Responsiveness to Modifying Gut Microbiota? A Double Blind Clinical Trial. *Front Neurol* 2018; 9: 662 [PMID: 30158897 DOI: 10.3389/fneur.2018.00662]
- Fischer M. Recent Research on Fecal Microbiota Transplantation in Inflammatory Bowel Disease Patients. *Gastroenterol Hepatol (NY)* 2019; 15: 44-47 [PMID: 30899209]
- Wang Z, Xu CM, Liu YX, Wang XQ, Zhang L, Li M, Zhu SW, Xie ZJ, Wang PH, Duan LP, Zhu HQ. Characteristic dysbiosis of gut microbiota of Chinese patients with diarrhea-predominant irritable bowel syndrome by an insight into the pan-microbiome. *Chin Med J (Engl)* 2019; 132: 889-904 [PMID: 30958430 DOI: 10.1097/CM9.000000000000192]
- Zhang B, Yue R, Chen Y, Yang M, Huang X, Shui J, Peng Y, Chin J. Gut Microbiota, a Potential New Target for Chinese Herbal Medicines in Treating Diabetes Mellitus. *Evid Based Complement Alternat Med* 2019; 2019: 2634898 [PMID: 30906411 DOI: 10.1155/2019/2634898]
- Pagliari D, Saviano A, Newton EE, Serricchio ML, Dal Lago AA, Gasbarrini A, Cianci R. Gut Microbiota-Immune System Crosstalk and Pancreatic Disorders. *Mediators Inflamm* 2018; 2018: 7946431 [PMID: 29563853 DOI: 10.1155/2018/7946431]
- Thomas RM, Jobin C. Microbiota in pancreatic health and disease: the next frontier in microbiome research. *Nat Rev Gastroenterol Hepatol* 2020; 17: 53-64 [PMID: 31811279 DOI: 10.1038/s41575-019-0242-7]
- Lerch MM, Gorelick FS. Models of acute and chronic pancreatitis. *Gastroenterology* 2013; 144: 1180-1193 [PMID: 23622127 DOI: 10.1053/j.gastro.2012.12.043]
- Zhang XM, Zhang ZY, Zhang CH, Wu J, Wang YX, Zhang GX. Intestinal Microbial Community Differs between Acute Pancreatitis Patients and Healthy Volunteers. *Biomed Environ Sci* 2018; 31: 81-86 [PMID: 29409589 DOI: 10.3967/bes2018.010]
- O'Boyle CJ, MacFie J, Mitchell CJ, Johnstone D, Sagar PM, Sedman PC. Microbiology of bacterial translocation in humans. *Gut* 1998; 42: 29-35 [PMID: 9505882 DOI: 10.1136/gut.42.1.29]
- Llorente C, Jepsen P, Inamine T, Wang L, Bluemel S, Wang HJ, Loomba R, Bajaj JS, Schubert ML, Sikaroodi M, Gillevet PM, Xu J, Kisseleva T, Ho SB, DePew J, Du X, Sørensen HT, Vilstrup H, Nelson KE, Brenner DA, Fouts DE, Schnabl B. Gastric acid suppression promotes alcoholic liver disease by inducing overgrowth of intestinal Enterococcus. *Nat Commun* 2017; 8: 837 [PMID: 29038503 DOI: 10.1038/s41467-017-00796-x]
- Sonika U, Goswami P, Thakur B, Yadav R, Das P, Ahuja V, Saraya A. Mechanism of Increased Intestinal Permeability in Acute Pancreatitis: Alteration in Tight Junction Proteins. *J Clin Gastroenterol* 2017; 51: 461-466 [PMID: 27466164 DOI: 10.1097/MCG.0000000000000612]
- Büchler MW, Gloor B, Müller CA, Friess H, Seiler CA, Uhl W. Acute necrotizing pancreatitis: treatment strategy according to the status of infection. *Ann Surg* 2000; 232: 619-626 [PMID: 11066131 DOI: 10.1097/00000658-200011000-00001]
- Isenmann R, Rüinzi M, Kron M, Kahl S, Kraus D, Jung N, Maier L, Malfertheiner P, Goebell H, Beger HG; German Antibiotics in Severe Acute Pancreatitis Study Group. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled, double-blind trial. *Gastroenterology* 2004; 126: 997-1004 [PMID: 15057739 DOI: 10.1053/j.gastro.2003.12.050]
- Tsitos GG, Luque-de León E, Söreide JA, Bannon MP, Zietlow SP, Baerga-Varela Y, Sarr MG. Management of necrotizing

- pancreatitis by repeated operative necrosectomy using a zipper technique. *Am J Surg* 1998; 175: 91-98 [PMID: 9515522 DOI: 10.1016/s0002-9610(97)00277-8]
- 21 Ahuja M, Schwartz DM, Tandon M, Son A, Zeng M, Swaim W, Eckhaus M, Hoffman V, Cui Y, Xiao B, Worley PF, Muallem S. Orai1-Mediated Antimicrobial Secretion from Pancreatic Acini Shapes the Gut Microbiome and Regulates Gut Innate Immunity. *Cell Metab* 2017; 25: 635-646 [PMID: 28273482 DOI: 10.1016/j.cmet.2017.02.007]
- 22 Gallo RL, Kim KJ, Bernfield M, Kozak CA, Zanetti M, Merluzzi L, Gennaro R. Identification of CRAMP, a cathelin-related antimicrobial peptide expressed in the embryonic and adult mouse. *J Biol Chem* 1997; 272: 13088-13093 [PMID: 9148921 DOI: 10.1074/jbc.272.20.13088]
- 23 Kościuczek EM, Lisowski P, Jarczak J, Strzałkowska N, Józwiak A, Horbańczyk J, Krzyżewski J, Zwierzchowski L, Bagnicka E. Cathelicidins: family of antimicrobial peptides. A review. *Mol Biol Rep* 2012; 39: 10957-10970 [PMID: 23065264 DOI: 10.1007/s11033-012-1997-x]
- 24 Bradley EL 3rd. A fifteen year experience with open drainage for infected pancreatic necrosis. *Surg Gynecol Obstet* 1993; 177: 215-222 [PMID: 8356492]
- 25 Haruta I, Yanagisawa N, Kawamura S, Furukawa T, Shimizu K, Kato H, Kobayashi M, Shiratori K, Yagi J. A mouse model of autoimmune pancreatitis with salivary gland involvement triggered by innate immunity via persistent exposure to avirulent bacteria. *Lab Invest* 2010; 90: 1757-1769 [PMID: 20733561 DOI: 10.1038/labinvest.2010.153]
- 26 Ukai T, Shikata S, Inoue M, Noguchi Y, Igarashi H, Isaji S, Mayumi T, Yoshida M, Takemura YC. Early prophylactic antibiotics administration for acute necrotizing pancreatitis: a meta-analysis of randomized controlled trials. *J Hepatobiliary Pancreat Sci* 2015; 22: 316-321 [PMID: 25678060 DOI: 10.1002/jhbp.221]
- 27 Oláh A, Belágyi T, Issekutz A, Gamal ME, Bengmark S. Randomized clinical trial of specific lactobacillus and fibre supplement to early enteral nutrition in patients with acute pancreatitis. *Br J Surg* 2002; 89: 1103-1107 [PMID: 12190674 DOI: 10.1046/j.1365-2168.2002.22511.x]
- 28 Qin HL, Zheng JJ, Tong DN, Chen WX, Fan XB, Hang XM, Jiang YQ. Effect of Lactobacillus plantarum enteral feeding on the gut permeability and septic complications in the patients with acute pancreatitis. *Eur J Clin Nutr* 2008; 62: 923-930 [PMID: 17579653 DOI: 10.1038/sj.ejcn.1602792]
- 29 Morrow LE, Gogineni V, Malesker MA. Synbiotics and probiotics in the critically ill after the PROPATRIA trial. *Curr Opin Clin Nutr Metab Care* 2012; 15: 147-150 [PMID: 22248590 DOI: 10.1097/MCO.0b013e32834fcea8]
- 30 Beyer G, Habtezion A, Werner J, Lerch MM, Mayerle J. Chronic pancreatitis. *Lancet* 2020; 396: 499-512 [PMID: 32798493 DOI: 10.1016/S0140-6736(20)31318-0]
- 31 Patel V, Willingham F. The Management of Chronic Pancreatitis. *Med Clin North Am* 2019; 103: 153-162 [PMID: 30466672 DOI: 10.1016/j.mcna.2018.08.012]
- 32 Lévy P, Domínguez-Muñoz E, Imrie C, Löhr M, Maisonneuve P. Epidemiology of chronic pancreatitis: burden of the disease and consequences. *United European Gastroenterol J* 2014; 2: 345-354 [PMID: 25360312 DOI: 10.1177/2050640614548208]
- 33 Witt H, Apte MV, Keim V, Wilson JS. Chronic pancreatitis: challenges and advances in pathogenesis, genetics, diagnosis, and therapy. *Gastroenterology* 2007; 132: 1557-1573 [PMID: 17466744 DOI: 10.1053/j.gastro.2007.03.001]
- 34 Han MM, Zhu XY, Peng YF, Lin H, Liu DC, Li L. The alterations of gut microbiota in mice with chronic pancreatitis. *Ann Transl Med* 2019; 7: 464 [PMID: 31700900 DOI: 10.21037/atm.2019.08.18]
- 35 Jandhyala SM, Madhulika A, Deepika G, Rao GV, Reddy DN, Subramanyam C, Sasikala M, Talukdar R. Altered intestinal microbiota in patients with chronic pancreatitis: implications in diabetes and metabolic abnormalities. *Sci Rep* 2017; 7: 43640 [PMID: 28255158 DOI: 10.1038/srep43640]
- 36 Louis P, Flint HJ. Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. *FEMS Microbiol Lett* 2009; 294: 1-8 [PMID: 19222573 DOI: 10.1111/j.1574-6968.2009.01514.x]
- 37 Wrzosek L, Miquel S, Noordine ML, Bouet S, Joncquel Chevalier-Curt M, Robert V, Philippe C, Bridonneau C, Cherbuy C, Robbe-Masselot C, Langella P, Thomas M. Bacteroides thetaiotaomicron and Faecalibacterium prausnitzii influence the production of mucus glycans and the development of goblet cells in the colonic epithelium of a gnotobiotic model rodent. *BMC Biol* 2013; 11: 61 [PMID: 23692866 DOI: 10.1186/1741-7007-11-61]
- 38 Martín R, Miquel S, Chain F, Natividad JM, Jury J, Lu J, Sokol H, Theodorou V, Bercik P, Verdu EF, Langella P, Bermúdez-Humarán LG. Faecalibacterium prausnitzii prevents physiological damages in a chronic low-grade inflammation murine model. *BMC Microbiol* 2015; 15: 67 [PMID: 25888448 DOI: doi:10.1186/s12866-015-0400-1]
- 39 Domínguez-Muñoz JE. Pancreatic exocrine insufficiency: diagnosis and treatment. *J Gastroenterol Hepatol* 2011; 26 Suppl 2: 12-16 [PMID: 21323992 DOI: 10.1111/j.1440-1746.2010.06600.x]
- 40 Nishiyama H, Nagai T, Kudo M, Okazaki Y, Azuma Y, Watanabe T, Goto S, Ogata H, Sakurai T. Supplementation of pancreatic digestive enzymes alters the composition of intestinal microbiota in mice. *Biochem Biophys Res Commun* 2018; 495: 273-279 [PMID: 29106956 DOI: 10.1016/j.bbrc.2017.10.130]
- 41 Grandier C, Adolph TE, Wieser V, Lowe P, Wrzosek L, Gyongyosi B, Ward DV, Grabherr F, Gerner RR, Pfister A, Enrich B, Ciocan D, Macheiner S, Mayr L, Drach M, Moser P, Moschen AR, Perlemuter G, Szabo G, Cassard AM, Tilg H. Recovery of ethanol-induced Akkermansia muciniphila depletion ameliorates alcoholic liver disease. *Gut* 2018; 67: 891-901 [PMID: 28550049 DOI: 10.1136/gutjnl-2016-313432]
- 42 Dos Santos PQ, Guedes JC, de Jesus RP, Santos RRD, Fiaccone RL. Effects of using symbiotics in the clinical nutritional evolution of patients with chronic pancreatitis: Study prospective, randomized, controlled, double blind. *Clin Nutr ESPEN* 2017; 18: 9-15 [PMID: 29132740 DOI: 10.1016/j.clnesp.2017.01.005]
- 43 Dylag K, Hubalewska-Mazgaj M, Surmiak M, Szmyd J, Brzozowski T. Probiotics in the mechanism of protection against gut inflammation and therapy of gastrointestinal disorders. *Curr Pharm Des* 2014; 20: 1149-1155 [PMID: 23755726 DOI: 10.2174/1381612811319990422]
- 44 Kawaguchi K, Koike M, Tsuruta K, Okamoto A, Tabata I, Fujita N. Lymphoplasmacytic sclerosing pancreatitis with cholangitis: a variant of primary sclerosing cholangitis extensively involving pancreas. *Hum Pathol* 1991; 22: 387-395 [PMID: 2050373 DOI: 10.1016/0046-8177(91)90087-6]
- 45 Yoshida K, Toki F, Takeuchi T, Watanabe S, Shiratori K, Hayashi N. Chronic pancreatitis caused by an autoimmune abnormality. Proposal of the concept of autoimmune pancreatitis. *Dig Dis Sci* 1995; 40: 1561-1568 [PMID: 7628283 DOI: 10.1007/BF02285209]
- 46 Hart PA, Zen Y, Chari ST. Recent Advances in Autoimmune Pancreatitis. *Gastroenterology* 2015; 149: 39-51 [PMID: 25770706 DOI: 10.1053/j.gastro.2015.03.010]
- 47 Sureka B, Rastogi A. Autoimmune Pancreatitis. *Pol J Radiol* 2017; 82: 233-239 [PMID: 28507644 DOI: 10.12659/PJR.900899]
- 48 Hamada S, Masamune A, Nabeshima T, Shimosegawa T. Differences in Gut Microbiota Profiles between Autoimmune Pancreatitis and Chronic Pancreatitis. *Tohoku J Exp Med* 2018; 244: 113-117 [PMID: 29434076 DOI: 10.1620/tjem.244.113]
- 49 Raderer M, Wrba F, Kornek G, Maca T, Koller DY, Weinlaender G, Hejna M, Scheithauer W. Association between Helicobacter pylori infection and pancreatic cancer. *Oncology* 1998; 55: 16-19 [PMID: 9428370 DOI: 10.1159/000011830]

- 50 Frulloni L, Lunardi C, Simone R, Dolcino M, Scattolini C, Falconi M, Benini L, Vantini I, Corrocher R, Puccetti A. Identification of a novel antibody associated with autoimmune pancreatitis. *N Engl J Med* 2009; 361: 2135-2142 [PMID: 19940298 DOI: 10.1056/NEJMoa0903068]
- 51 Khan J, Pelli H, Lappalainen-Lehto R, Järvinen S, Sand J, Nordback I. Helicobacter pylori in alcohol induced acute pancreatitis. *Scand J Surg* 2009; 98: 221-224 [PMID: 20218418 DOI: 10.1177/145749690909800405]
- 52 Risch HA, Lu L, Kidd MS, Wang J, Zhang W, Ni Q, Gao YT, Yu H. Helicobacter pylori seropositivities and risk of pancreatic carcinoma. *Cancer Epidemiol Biomarkers Prev* 2014; 23: 172-178 [PMID: 24234587 DOI: 10.1158/1055-9965.EPI-13-0447]
- 53 Guarneri F, Guarneri C, Benvenia S. Helicobacter pylori and autoimmune pancreatitis: role of carbonic anhydrase via molecular mimicry? *J Cell Mol Med* 2005; 9: 741-744 [PMID: 16202223 DOI: 10.1111/j.1582-4934.2005.tb00506.x]
- 54 Arai Y, Yamashita K, Kuriyama K, Shiokawa M, Kodama Y, Sakurai T, Mizugishi K, Uchida K, Kadowaki N, Takaori-Kondo A, Kudo M, Okazaki K, Strober W, Chiba T, Watanabe T. Plasmacytoid Dendritic Cell Activation and IFN- α Production Are Prominent Features of Murine Autoimmune Pancreatitis and Human IgG4-Related Autoimmune Pancreatitis. *J Immunol* 2015; 195: 3033-3044 [PMID: 26297761 DOI: 10.4049/jimmunol.1500971]
- 55 Watanabe T, Yamashita K, Arai Y, Minaga K, Kamata K, Nagai T, Komeda Y, Takenaka M, Hagiwara S, Ida H, Sakurai T, Nishida N, Strober W, Kudo M. Chronic Fibro-Inflammatory Responses in Autoimmune Pancreatitis Depend on IFN- α and IL-33 Produced by Plasmacytoid Dendritic Cells. *J Immunol* 2017; 198: 3886-3896 [PMID: 28373582 DOI: 10.4049/jimmunol.1700060]
- 56 Kamata K, Watanabe T, Minaga K, Strober W, Kudo M. Autoimmune Pancreatitis Mouse Model. *Curr Protoc Immunol* 2018; 120: 15.31.1-15.31.8 [PMID: 29512140 DOI: 10.1002/cpim.41]
- 57 Kamata K, Watanabe T, Minaga K, Hara A, Yoshikawa T, Okamoto A, Yamao K, Takenaka M, Park AM, Kudo M. Intestinal dysbiosis mediates experimental autoimmune pancreatitis via activation of plasmacytoid dendritic cells. *Int Immunol* 2019; 31: 795-809 [PMID: 31287532 DOI: 10.1093/intimm/dxz050]
- 58 中华医学会消化病学分会胰腺疾病学组, 《中华胰腺病杂志》编委会, 《中华消化杂志》编委会. 中国急性胰腺炎诊治指南(2019年, 沈阳). 临床肝胆病杂志 2019; 35: 2706-2711 [DOI: 10.3969/j.issn.1001-5256.2019.12.013]
- 59 Meijerink M, van Hemert S, Taverne N, Wels M, de Vos P, Bron PA, Savelkoul HF, van Bilsen J, Kleerebezem M, Wells JM. Identification of genetic loci in Lactobacillus plantarum that modulate the immune response of dendritic cells using comparative genome hybridization. *PLoS One* 2010; 5: e10632 [PMID: 20498715 DOI: 10.1371/journal.pone.0010632]
- 60 Macho Fernandez E, Valenti V, Rockel C, Hermann C, Pot B, Boneca IG, Grangette C. Anti-inflammatory capacity of selected lactobacilli in experimental colitis is driven by NOD2-mediated recognition of a specific peptidoglycan-derived muropeptide. *Gut* 2011; 60: 1050-1059 [PMID: 21471573 DOI: 10.1136/gut.2010.232918]
- 61 Cui LH, Wang XH, Peng LH, Yu L, Yang YS. [The effects of early enteral nutrition with addition of probiotics on the prognosis of patients suffering from severe acute pancreatitis]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2013; 25: 224-228 [PMID: 23660099 DOI: 10.3760/cma.j.issn.2095-4352.2013.04.011]
- 62 Gou S, Yang Z, Liu T, Wu H, Wang C. Use of probiotics in the treatment of severe acute pancreatitis: a systematic review and meta-analysis of randomized controlled trials. *Crit Care* 2014; 18: R57 [PMID: 24684832 DOI: 10.1186/cc13809]

科学编辑: 张砚梁 制作编辑: 张砚梁



ISSN 1009-3079 (print) ISSN 2219-2859 (online) DOI: 10.11569 © 2021 Baishideng Publishing Group Inc.
All rights reserved.

• 消息 •

《世界华人消化杂志》参考文献要求

本刊讯 本刊采用“顺序编码制”的著录方法,即以文中出现顺序用阿拉伯数字编号排序。提倡对国内同行近年已发表的相关研究论文给予充分的反映,并在文内引用处右上角加方括号注明角码。文中如列作者姓名,则需在“Pang等”的右上角注角码号;若正文中仅引用某文献中的论述,则在该论述的句末右上角注角码号。如马连生^[1]报告……,研究^[2-5]认为……;PCR方法敏感性高^[6,7]。文献序号作正文叙述时,用与正文同号的数字并排,如本实验方法见文献[8]。所引参考文献必须以近2-3年SCIE, PubMed,《中国科技论文统计源期刊》和《中文核心期刊要目总览》收录的学术类期刊为准,通常应只引用与其观点或数据密切相关的国内外期刊中的最新文献,包括世界华人消化杂志(<http://www.wjgnet.com/1009-3079/index.jsp>)和World Journal of Gastroenterology(<http://www.wjgnet.com/1007-9327/index.jsp>)。期刊: 序号, 作者(列出全体作者)。文题, 刊名, 年, 卷, 起页-止页, PMID编号; 书籍: 序号, 作者(列出全部), 书名, 卷次, 版次, 出版地, 出版社, 年, 起页-止页。



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
https://www.wjgnet.com



ISSN 1009-3079

