ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2024 May 15; 16(5): 1676-2263

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Oncology

Contents

Monthly Volume 16 Number 5 May 15, 2024

EDITORIAL

1676 Interleukin-1β: Friend or foe for gastrointestinal cancers

Khawkhiaw K, Panaampon J, Imemkamon T, Saengboonmee C

1683 Overcoming geographical and socioeconomic limitations in colorectal cancer screening

Rozani S, Lykoudis PM

REVIEW

1690 Mechanisms of myeloid-derived suppressor cell-mediated immunosuppression in colorectal cancer and related therapies

Nie SC, Jing YH, Lu L, Ren SS, Ji G, Xu HC

1705 Impact of STAT-signaling pathway on cancer-associated fibroblasts in colorectal cancer and its role in immunosuppression

Sánchez-Ramírez D, Mendoza-Rodríguez MG, Alemán OR, Candanedo-González FA, Rodríguez-Sosa M, Montesinos-Montesinos JJ, Salcedo M, Brito-Toledo I, Vaca-Paniagua F, Terrazas LI

MINIREVIEWS

1725 Advances in the study of gastric organoids as disease models

Liu YY, Wu DK, Chen JB, Tang YM, Jiang F

ORIGINAL ARTICLE

Case Control Study

1737 Evaluation of the value of combined detection of tumor markers CA724, carcinoembryonic antigen, CA242, and CA19-9 in gastric cancer

Zhou CM, Zhao SH

Retrospective Cohort Study

1745 Different lymph node staging systems for predicting the prognosis of colorectal neuroendocrine neoplasms

Zhang YY, Cai YW, Zhang X

1756 Pancreatic neuroendocrine tumors: Are tumors smaller than 2 cm truly indolent?

Hoyos S, Posada-Moreno P, Guzman-Arango N, Chanci-Drago R, Chavez J, Andrés-Duarte A, Salazar-Ochoa S

1763 Albumin–bilirubin grade as a predictor of survival in hepatocellular carcinoma patients with thrombocytopenia

Man ZR, Gong XK, Qu KL, Pang Q, Wu BQ

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 5 May 15, 2024

Contents

1773 TRIANGLE operation, combined with adequate adjuvant chemotherapy, can improve the prognosis of pancreatic head cancer: A retrospective study

Chen JH, Zhu LY, Cai ZW, Hu X, Ahmed AA, Ge JQ, Tang XY, Li CJ, Pu YL, Jiang CY

1787 Prognostic relevance of ventricular arrhythmias in surgical patients with gastrointestinal tumors

Xue JJ, Hu ST, Wang CC, Chen ZC, Cheng SY, Yu SQ, Peng HJ, Zhang YT, Zeng WJ

Retrospective Study

1796 Diagnostic performance of dynamic contrast-enhanced magnetic resonance imaging parameters and serum tumor markers in rectal carcinoma prognosis

Mu RQ, Lv JW, Ma CY, Ma XH, Xing D, Ma HS

1808 Nomogram prediction of vessels encapsulating tumor clusters in small hepatocellular carcinoma ≤ 3 cm based on enhanced magnetic resonance imaging

Chen HL, He RL, Gu MT, Zhao XY, Song KR, Zou WJ, Jia NY, Liu WM

1821 Percutaneous transhepatic cholangioscopy-assisted biliary polypectomy for local palliative treatment of intraductal papillary neoplasm of the bile duct

Ren X, Qu YP, Zhu CL, Xu XH, Jiang H, Lu YX, Xue HP

1833 Perioperative remedial antiviral therapy in hepatitis B virus-related hepatocellular carcinoma resection: How to achieve a better outcome

Mu F, Hu LS, Xu K, Zhao Z, Yang BC, Wang YM, Guo K, Shi JH, Lv Y, Wang B

1849 Magnetic resonance imaging-based lymph node radiomics for predicting the metastasis of evaluable lymph nodes in rectal cancer

Ye YX, Yang L, Kang Z, Wang MQ, Xie XD, Lou KX, Bao J, Du M, Li ZX

1861 Is sarcopenia effective on survival in patients with metastatic gastric cancer?

Dogan O, Sahinli H, Duzkopru Y, Akdag T, Kocanoglu A

1869 Clinical outcome and prognostic factors of T4N0M0 colon cancer after R0 resection: A retrospective study

Liu B, Zhang ZX, Nie XY, Sun WL, Yan YJ, Fu WH

Observational Study

1878 Correlation of tumor-associated macrophage density and proportion of M2 subtypes with the pathological stage of colorectal cancer

Fazal F, Khan MA, Shawana S, Rashid R, Mubarak M

Clinical and Translational Research

1890 SERPINH1 promoted the proliferation and metastasis of colorectal cancer by activating PI3K/Akt/mTOR signaling pathway

Jin XS, Chen LX, Ji TT, Li RZ

1908 Four centrosome-related genes to predict the prognosis and drug sensitivity of patients with colon cancer

Wang HY, Diao Y, Tan PZ, Liang H

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 5 May 15, 2024

Contents

1925 METTL5 promotes gastric cancer progression *via* sphingomyelin metabolism

Zhang YQ, Li J, Qin Z, Li DM, Ye FZ, Bei SH, Zhang XH, Feng L

1947 Identification of differentially expressed mRNAs as novel predictive biomarkers for gastric cancer diagnosis and prognosis

Zhou JW, Zhang YB, Huang ZY, Yuan YP, Jin J

1965 To explore the mechanism of Yigong San anti-gastric cancer and immune regulation

Lu DD, Yuan L, Wang ZZ, Zhao JJ, Du YH, Ning N, Chen GQ, Huang SC, Yang Y, Zhang Z, Nan Y

1995 Casual associations between blood metabolites and colon cancer

Hu KY, Cheng YQ, Shi ZL, Ren FP, Xiao GF

Basic Study

2006 METTL5 promotes cell proliferation, invasion, and migration by up-regulating Toll-like receptor 8 expression in colorectal cancer

Kong LS, Tao R, Li YF, Wang WB, Zhao X

2018 Predictive model using four ferroptosis-related genes accurately predicts gastric cancer prognosis

Wang L, Gong WH

2038 Novel miR-490-3p/hnRNPA1-b/PKM2 axis mediates the Warburg effect and proliferation of colon cancer cells *via* the PI3K/AKT pathway

Wan XH, Jin GB, Yang Q, Hu JL, Liu ZL, Rao J, Wen C, Li PL, Yang XM, Huang B, Wang XZ

2060 Epigenetic silencing schlafen-11 sensitizes esophageal cancer to ATM inhibitor

Zhou J, Zhang MY, Gao AA, Zhu C, He T, Herman JG, Guo MZ

2074 Transglutaminase 2 serves as a pathogenic hub gene of KRAS mutant colon cancer based on integrated analysis

Peng WB, Li YP, Zeng Y, Chen K

2091 Plexin domain-containing 1 may be a biomarker of poor prognosis in hepatocellular carcinoma patients, may mediate immune evasion

Tang MY, Shen X, Yuan RS, Li HY, Li XW, Jing YM, Zhang Y, Shen HH, Wang ZS, Zhou L, Yang YC, Wen HX, Su F

2113 Immunomodulation of adipose-derived mesenchymal stem cells on peripheral blood mononuclear cells in colorectal cancer patients with COVID-19

Wang JF, Yang XX, Zhang J, Zheng Y, Zhang FQ, Shi XF, Wang YL

2123 *MiRNA-145-5p* inhibits gastric cancer progression *via* the serpin family E member 1- extracellular signal-regulated kinase-1/2 axis

Bai HX, Qiu XM, Xu CH, Guo JQ

SYSTEMATIC REVIEWS

2141 Systematic review of risk factors, prognosis, and management of colorectal signet-ring cell carcinoma

Nuytens F, Drubay V, Eveno C, Renaud F, Piessen G

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 5 May 15, 2024

Contents

META-ANALYSIS

2159 Loss of heterozygosity for chromosomes 16q in Wilms tumors predicts outcomes: A meta-analysis

Song YH, Li WL, Yang Z, Gao Y, Feng ZP

2168 Association of complement components with risk of colorectal cancer: A systematic review and meta-analysis

Zhu XL, Zhang L, Qi SX

SCIENTOMETRICS

2181 Mapping the intellectual structure and emerging trends for the application of nanomaterials in gastric cancer: A bibliometric study

Liu BN, Gao XL, Piao Y

2200 Hotspots and trends of risk factors in gastric cancer: A visualization and bibliometric analysis

Li M, Gao N, Wang SL, Guo YF, Liu Z

CASE REPORT

2219 Chemoradiotherapy plus tislelizumab for mismatch repair proficient rectal cancer with supraclavicular lymph node metastasis: A case report

Zhong WT, Lv Y, Wang QY, An R, Chen G, Du JF

2225 Multidisciplinary comprehensive treatment of massive hepatocellular carcinoma with hemorrhage: A case report and review of literature

Kou XS, Li FF, Meng Y, Zhao JM, Liu SF, Zhang L

2233 Metastatic pancreatic and lung cancer patient in complete remission following immunotherapy: A case report and review of literature

Martínez-Galán J, Jiménez-Luna C, Rodriguez I, Maza E, García-Collado C, Rodríguez-Fernández A, López-Hidalgo JL, Caba O

2241 Hepatocellular carcinoma presenting as an extrahepatic mass: A case report and review of literature

Wu WK, Patel K, Padmanabhan C, Idrees K

2253 Undifferentiated high-grade pleomorphic sarcoma of the common bile duct: A case report and review of literature

Zheng LP, Shen WY, Hu CD, Wang CH, Chen XJ, Wang J, Shen YY

LETTER TO THE EDITOR

2261 Hemostatic radiotherapy for bleeding gastrointestinal tumors

Rao V, Singh S, Zade B

ABOUT COVER

Peer Reviewer of *World Journal of Gastrointestinal Oncology*, Andreia Albuquerque, MD, PhD, Gastroenterologist, Professor, Research Scientist, Precancerous Lesions and Early Cancer Management Research Group RISE@CI-IPO (Health Research Network), Portuguese Oncology Institute of Porto (IPO-Porto), Porto 4200-072, Portugal. a.albuquerque.dias@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJGO* as 3.0; IF without journal self cites: 2.9; 5-year IF: 3.0; Journal Citation Indicator: 0.49; Ranking: 157 among 241 journals in oncology; Quartile category: Q3; Ranking: 58 among 93 journals in gastroenterology and hepatology; and Quartile category: Q3. The *WJGO*'s CiteScore for 2022 is 4.1 and Scopus CiteScore rank 2022: Gastroenterology is 71/149; Oncology is 197/366.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Xiang-Di Zhang*; **Production Department Director:** *Xiang Li*; **Cover Editor:** *Jia-Ru Fan*.

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5204/editorialboard.htm

PUBLICATION DATE
May 15, 2024

COPYRIGHT
© 2024 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

© 2024 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
E-mail: office@baishideng.com https://www.wjgnet.com

World Journal of Gastrointestinal Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Oncol 2024 May 15; 16(5): 1676-1682

DOI: 10.4251/wjgo.v16.i5.1676

ISSN 1948-5204 (online)

EDITORIAL

Interleukin-1β: Friend or foe for gastrointestinal cancers

Kullanat Khawkhiaw, Jutatip Panaampon, Thanit Imemkamon, Charupong Saengboonmee

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Sivaraj N, India

Received: December 27, 2023
Peer-review started: December 27, 2023
First decision: February 5, 2024
Revised: February 17, 2024
Accepted: March 19, 2024
Article in press: March 19, 2024
Published online: May 15, 2024

Kullanat Khawkhiaw, Charupong Saengboonmee, Department of Biochemistry, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

Kullanat Khawkhiaw, Charupong Saengboonmee, Center for Translational Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

Kullanat Khawkhiaw, Charupong Saengboonmee, Cholangiocarcinoma Research Institute, Khon Kaen University, Khon Kaen 40002, Thailand

Jutatip Panaampon, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02215, United States

Jutatip Panaampon, Department of Medicine, Harvard Medical School, Boston, MA 02215, United States

Jutatip Panaampon, Division of Hematopoiesis, Joint Research Center for Human Retrovirus Infection, Kumamoto University, Kumamoto 860-0811, Japan

Thanit Imemkamon, Department of Medicine, Faculty of Medicine, Khon Kaen Univsersity, Khon Kaen 40002, Thailand

Corresponding author: Charupong Saengboonmee, MD, PhD, Assistant Professor, Doctor, Department of Biochemistry, Faculty of Medicine, Khon Kaen University, 123 Mittraphap Highway, Khon Kaen 40002, Thailand. charusa@kku.ac.th

Abstract

Gastrointestinal (GI) cancer is a malignancy arising in the digestive system and accounts for approximately a third of increasing global cancer-related mortality, especially in the colorectum, esophagus, stomach, and liver. Interleukin-1β (IL-1β) is a leukocytic pyrogen recognized as a tumor progression-related cytokine. IL-1β secretion and maturation in inflammatory responses could be regulated by nuclear factor-kappaB-dependent expression of NLR family pyrin domain containing 3, inflammasome formation, and activation of IL-1 converting enzyme. Several studies have documented the pro-tumorigenic effects of IL-1β in tumor microenvironments, promoting proliferation and metastatic potential of cancer cells *in vitro* and tumorigenesis *in vivo*. The application of IL-1β inhibitors is also promising for targeted therapy development in some cancer types. However, as a leukocytic pro-inflammatory cytokine, IL-1β may also possess anti-tumorigenic effects and be type-specific in different cancers. This editorial discusses the up-to-date roles of IL-1β in GI cancers, including underlying mechanisms and downstream signaling pathways. Understanding and clarifying the roles of IL-1β would

significantly benefit future therapeutic targeting and help improve therapeutic outcomes in patients suffering from GI cancer.

Key Words: Cancer; Gastrointestinal tract; Inflammation; Interleukin-1β; Tumor microenvironment

©The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Interleukin-1β (IL-1β) is a pro-inflammatory cytokine primarily secreted by leukocytes to activate the immune response at the site of infection or inflammation. As tumor-promoting inflammation is one of the cancer hallmarks, IL-1β then plays central roles in tumor-promoting activities in many cancers, including cancers of the gastrointestinal tract. On the other hand, by activating and recruiting immune cells into the tumor microenvironments, IL-1β also has anti-tumor effects depending on the subtypes of immune cells that respond and infiltrate into the tumor site. Whether it could be a promising target for future therapeutic development is then discussed in this article.

Citation: Khawkhiaw K, Panaampon J, Imemkamon T, Saengboonmee C. Interleukin-1β: Friend or foe for gastrointestinal cancers. *World J Gastrointest Oncol* 2024; 16(5): 1676-1682
URL: https://www.wjgnet.com/1948-5204/full/v16/i5/1676.htm
DOI: https://dx.doi.org/10.4251/wjgo.v16.i5.1676

INTRODUCTION

Tumor microenvironments are composed of various cell populations, not only the cancer cells themselves but also others, *e.g.*, fibroblasts, endothelial cells, and infiltrated white blood cells[1]. The infiltrated white blood cells or immune cells that reside in the tumors create a biological niche in the so-called tumor immune microenvironment that interacts with the cancer cells *via* signals between cancer and immune cell communities. This communication between immune and cancer cells could direct the progression or recession of cancers depending on the subtypes of immune cells and the "media" of communication. The proinflammatory cytokine interleukin-1β (IL-1β) has a recognized central inflammatory signaling role in innate immunity in tissues and has been questioned for decades whether it possesses pro- or anti-tumorigenic effects[2]. As a player in innate immunity, IL-1β potentially possesses anti-tumor effects by activating antigen-presenting cells and phagocytes. However, this cytokine can be produced and released by both cancer cells and other cells in tumor microenvironments, suggesting different functions in tumor biology. Thus, IL-1β's actual roles have been investigated extensively in gastrointestinal (GI) cancers for guidance in developing novel therapeutic methods.

IL-1β SIGNALING

IL-1β, an influential pro-inflammatory cytokine, is synthesized and secreted by various cell types in tumor microenvironments[2], such as white blood cells, cancer-associated fibroblasts (CAFs), and cancer cells. Signaling of IL-1β was conventionally initiated by binding to interleukin-1 receptor (IL-1R) type 1 (IL-1R1), which presents three extra-cellular immunoglobulin binding domains and is associated with the highly homologous IL-1R accessory protein (IL-1RAcP or IL-1R3). These signaling functions can be controlled by several cell-secreted inhibitors, such as IL-1 receptor antagonist (IL-1RA), IL-1 receptor type II (IL-1RII), and other soluble receptors[3]. Upon activation, IL-1R/IL1-RAcP recruits myeloid differentiation primary response 88 (Myd88) through Toll/interleukin-1 receptor/resistance protein domains (Figure 1). Then, MyD88 associates with interleukin 1 receptor-associated kinase (IRAK) 1, IRAK 2, and IRAK4. IRAK4 then phosphorylates IRAK1 and IRAK2 to enable their association with tumor necrosis factor receptor 6, which further recruits and activates the transforming growth factor β-activated kinase 1 (TAK1). TAK1 then activates p38 and c-Jun N-terminal kinase, leading to the activation of the inhibitor nuclear factor-kappaB (NF-κB) kinase complex. This subsequently degrades the inhibitor of NF-κB, rendering NF-κB translocation from the cytosol into the nucleus[2,4]. IL-1β signaling plays various roles in cancer progression and malignancy, such as serving as an inducer of carcinogenesis, angiogenesis, and metastasis (Figure 1)[5]. Careful consideration is, then, needed when it is proposed as the therapeutic target for cancers.

ROLES OF IL-1β IN GI CANCERS

GI cancers include malignancies along the alimentary tracts (esophagus, stomach, small intestine, colon-rectum, and anus) and the digestive accessory organs (liver, pancreas, and biliary tracts). It is the most common cancer group affecting both males and females worldwide. In this article, the roles of IL-1β in different types of GI cancer are reviewed and discussed.

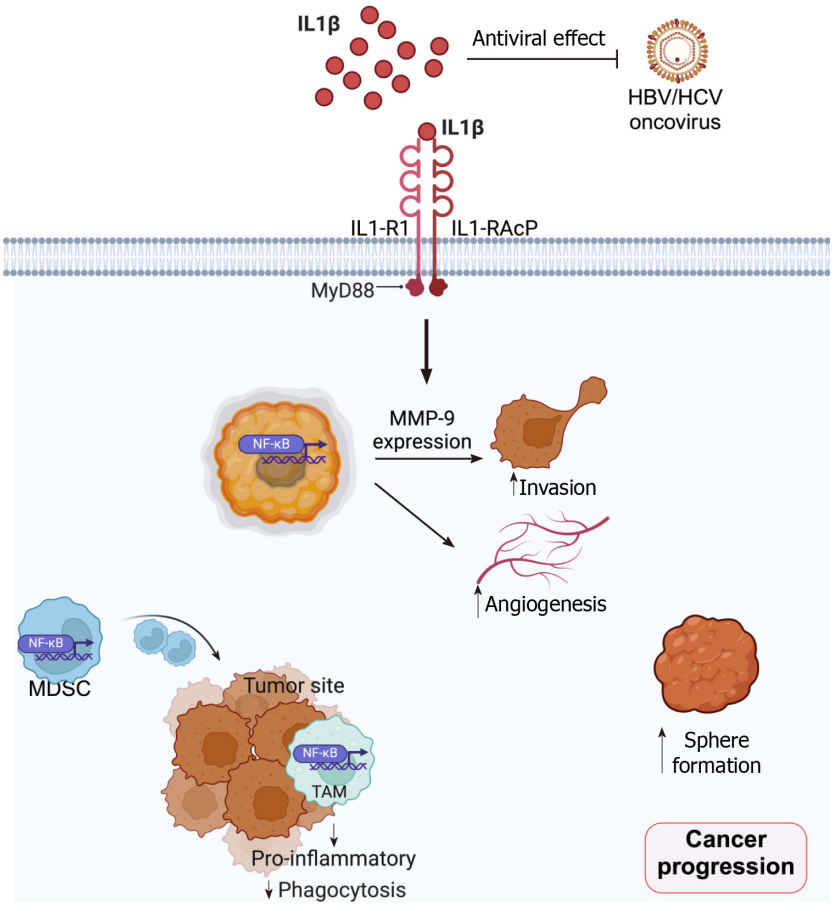

Figure 1 Schematic summary of roles of interleukin-1β in cancer progression. Interleukin-1β (IL-1β) has an anti-hepatitis B virus/hepatitis C virus effect, which leads to a reduced risk of liver cancer. In contrast, IL-1β activates the nuclear factor-kappaB (NF-κB) signaling pathway in both cancer cells and immune cells, including myeloid-derived suppressor cells (MDSC) and tumor-associated macrophages (TAM). NF-κB activation in cancer cells triggers matrix metalloproteinase 9 expression and promotes invasion, angiogenesis as well as sphere formation. Activation of the NF-κB signaling pathway in MDSC increases MDSC migration and infiltration to the tumor site, which further inhibits effector immune cells and promotes cancer progression. Moreover, NF-κB induction reduces the phagocytotic activity of TAM in the tumor site (Created by BioRender). IL-1β: Interleukin-1β; HBV: Hepatitis B virus; HCV: Hepatitis C virus; MDSC: Myeloid-derived suppressor cells; NF-κB: Nuclear factor-kappaB; TAM: Tumor-associated macrophages; MMP-9: Matrix metalloproteinase 9; Myd88: Myeloid differentiation primary response 88.

Esophageal cancer

Expression analysis based on a dataset indicated significantly elevated expression levels of IL-1β in esophageal cancer cases compared to normal samples[6]. A positive immunohistochemistry score for IL-1β correlated with a diminished response to neoadjuvant therapy and poorer overall survival among patients with esophageal squamous cell carcinoma (ESCC)[7]. In the context of ESCC, investigations revealed that the overexpression of IL-1RA, conversely, curtailed the proliferation, migration, and lymphangiogenesis of ESCC cells. This effect was attributed to the downregulation of vascular endothelial growth factor-C and matrix metalloproteinase 9 (MMP-9). Downregulation of IL-1RA was also observed in esophageal carcinomas[8]. Furthermore, *in vivo* assessments demonstrated a significant reduction in the growth rate of ESCC upon IL-1RA overexpression[9]. In another *in vivo* model, IL-1β transgenic mice exhibited inflammation-driven, age-dependent progression toward malignancy of the esophagus, characterized by squamous epithelial hyperplasia, dysplasia, and finally ESCC. Notably, this inflammation-based progression occurred independently of the gut microbiome[10]. Within the transgenic L2-IL1B mice cohort subjected to a high-fat diet to promote inflammation-based progressive esophageal adenocarcinoma[11], IL-1R antagonist and anti-inflammatory agent administration significantly diminished inflammatory scores and also led to a reduction in metaplasia and dysplasia scores in L2-IL1B mice exposed to a high-fat diet. All these findings emphasize the significant roles of IL-1β as a linking cytokine for chronic inflammation and esophageal cancer in both histological subtypes of squamous cell carcinoma and adenocarcinoma.

Gastric cancer

IL-1β exerts a multifaceted influence on the development and progression of gastric cancer, primarily through its capacity to inhibit gastric acid secretion, induce epigenetic alterations, facilitate angiogenesis, attract adhesive factors, and release various inflammatory mediators[12]. A meta-analysis revealed an association between *IL-1B−511C/T* polymorphisms and susceptibility to an intestinal subtype of gastric adenocarcinoma[13]. Within gastric carcinoma cell lines, such as BGC-823, IL-1β was observed to upregulate retinoid X receptors *via* the activation of NF-κB signaling pathways[14]. Additionally, IL-1β enhanced NF-κB activation, MMP-9 expression, and invasive capabilities of gastric cancer cells[15]. The gastric-

specific overexpression of human IL-1β in transgenic mice was demonstrated to be sufficient for the progression of gastric dysplasia to cancer. Moreover, the activation of NF-κB in myeloid-derived suppressor cells (MDSCs) was significantly associated with cancer development. Notably, blockade by IL-1RA significantly impeded histological progression and diminished MDSC recruitment[16]. Examining the tumor microenvironment, the majority of tumor-associated macrophages (TAMs) exhibit expression of proinflammatory cytokine/chemokine genes, including *IL1B, CCL2, CCL3,* and *CCL20.* IL-1β and its decoy receptor IL1-R2 are also the most abundant cytokine–receptor pair interaction between TAMs and tumor cells. This suggests a potential mechanism where tumor cells can be inhibited by targeting IL-1β-mediated proinflammatory signaling within the tumor microenvironment[17].

Colorectal cancer

Polymorphic variations within the *IL1B* gene, concomitant with heightened levels of IL-1β, have been significantly associated with an augmented susceptibility to the development of colon cancer[18]. Conversely, single-nucleotide polymorphisms associated with the expression of IL-1RA have been linked to the enhanced survival of patients with colorectal cancer (CRC)[19]. A meta-analysis demonstrated that *IL-1α rs3783553*, *IL-1β + 31C/T*, *IL-1β + 511C/T*, and *IL-1RN VNTR* are critical genes for CRC susceptibility[20]. Noteworthy, serum levels of IL-1β exhibited a significant upregulation in patients with CRC when compared to healthy controls[21]. The addition of IL-1β to the culture medium was found to significantly augment the sphere-forming capability and invasive potential of colon cancer cell lines[22] induction by IL-1β and was also associated with an increased expression of the epithelial-mesenchymal transition activator, Zinc finger E-box-binding homeobox 1, in IL-1β-induced spheres. In colonic CAFs, IL-1β initiated pro-tumorigenic signaling, leading to the nuclear translocation of NK-κB p65 and subsequent enhancement of tumor growth *in vitro*[23]. Targeting basal IL-1β crosstalk between CAFs and colorectal tumor cells may also inhibit the pro-tumorigenic function of CAFs. IL-1β has also been shown to have pro-tumorigenic effects *via* activation of NF-κB and miR-181a[24]. IL-1β activated NF-κB and miR-181a, which further repressed phosphatase and tensin homolog, a ubiquitous tumor-suppressor gene implicated in various solid tumors and immune responses[25-27]. Conversely, the anti-tumorigenic effect of IL-1β has also been reported in colon cancer. Increased tumor burden was correlated with attenuated levels of IL-1β and IL-18 at the tumor sites[28]. A protective role of IL-1β was demonstrated in mouse models of chemically induced colitis and colon cancer[29]. Two variants of the *IL1B* gene, including *rs1143623* and *rs1143634* polymorphisms, were associated with decreased risk, more favorable clinical features, and better overall survival of CRC than the wild type [30]. Different study models have resulted in diverse effects of IL-1β in CRC development and progression. Thus, the roles of IL-1β remain unclear in CRC and need further investigation.

Liver cancers

The examination of allele frequencies pertaining to *IL-1B-511* revealed significant elevations among individuals afflicted with hepatitis B virus-associated hepatocellular carcinoma (HCC) compared to healthy controls[31]. Notably, within hepatitis C-infected individuals, the *IL-1B-511* genotype T/T emerged as a risk factor for HCC. Polymorphic variations within the *IL-1B-511* genetic locus were raised as possible risk factors for HCC development[32]. Mechanistically, miR-4756 inhibition reversed the effects induced by circUBAP2 silencing on the IL-17 and IL-1β levels and HCC cell migration [33]. Orthotopic liver tumor models and RNA-sequencing demonstrated a pivotal role for pulmonary IL-1β in creating a permissive lung pre-metastatic niche *via* enhancing MMP-9 expression and recruiting myeloid cells, thus promoting pulmonary metastasis of HCC[34]. In contrast, the hepatitis B virus modulated liver macrophage function to favor the establishment and likely maintenance of infection. It impaired the production of IL-1β, playing roles as antiviral cytokines, while promoting that of IL-10 in the microenvironment[35]. An *in vitro* model revealed that anakinra, an IL-1R1 antagonist, reversed IL-1β-promoted HCC metastasis[36]. IL-1β can promote TAMs and MDSCs infiltration *via* induction of solute carrier family 7-member 11 overexpression, thus up-regulating programmed death-ligand 1 and colony-stimulating factor 1 through the α-ketoglutarate/hypoxia-inducible factor 1 subunit alpha axis. These result in homeobox protein Hox-C10 overexpression and exacerbate HCC metastasis through the upregulation of phosphoinositide-dependent kinase-1 and vasodilator-stimulated phosphoprotein[37]. IL-1β/IRAK-1 inflammatory signaling can also promote an oncoprotein ankyrin, which is activated during hepatocarcinogenesis[38]. In summary, although IL-1β exerted anti-viral effects on the carcinogenic virus hepatitis B and C, IL-1β then turned out to be a "friend" for HCC, promoting growth and metastasis and avoiding the effects of anti-tumor immunity when hepatocytes turn malignant.

Pancreatic cancer

IL-1β expression in pancreatic tumors was associated with shorter survival of patients with pancreatic ductal adenocarcinoma (PDAC)[39]. Physical proximity with IL-1β$^+$ TAMs was associated with inflammatory reprogramming and acquisition of pathogenic properties by a subset of PDAC cells[40]. Inhibiting IL-1β activity caused TAM reprogramming and antagonized tumor cell inflammation, leading to PDAC control *in vivo*. Tumor cell-derived IL-1β regulated an immune-modulatory program that supported pancreatic tumorigenesis[41]. IL-1β also served as a key cytokine that activated IRAK4 in pancreatic CAF[42,43]. Targeting IRAK4 or IL-1β thus rendered PDAC less fibrotic and more sensitive to gemcitabine *in vivo*.

Gallbladder cancer

IL-1β expression was significantly upregulated in gallbladder cancer (GBC) cases as compared with non-malignant cholelithiasis controls[44]. The study also showed that levels of IL-6, IL-1β, and IL-23 were significantly higher in GBC patients, whereas transforming growth factor-β was lower compared with healthy individuals[45]. In a north Indian population, the haplotype 1/C of *IL1B* was found to confer a significantly enhanced risk of GBC in patients with

gallstones[46]. Exogenous IL-1β promoted the proliferation of GBC-SD and SGC996 cells *in vitro* and *in vivo* and also promoted migration *in vitro via* TWIST activation[47]. To date, most studies in GBC point toward the roles of IL-1β as a pro-tumorigenic cytokine; however, studies on the roles and clinical significance of IL-1R are still lacking.

Bile duct cancer

A genetic polymorphism study revealed that the *IL-1B +3954 C/C* genotype was associated with a shorter overall survival in patients with resected intrahepatic cholangiocarcinoma, as determined by both univariable and multivariable analyses. The *IL-1B +3954* polymorphism was also associated with shorter disease-free survival[48]. Further, monocytes from patients with primary sclerosing cholangitis, a condition most commonly linked to bile duct cancer[49], produced significantly more IL-1β and IL-6[50]. However, the roles of IL-1β in bile duct cancer progression and their underlying mechanisms remain under-investigated. This is still the missing piece of the jigsaw in the study of IL-1β's effects on the tumor biology of GI cancers.

CONCLUSION

Although IL-1β plays central roles in inflammation and innate immunity that could potentially be a foe for retarding tumorigenesis and tumor cell progression, it is likely to become a friend for cancer cells in most GI cancers. Still, IL-1β possesses anti-tumor effects in some subtypes of cancers, possibly because of the underlying tumor microenvironments. The current understanding of IL-1β's roles in GI cancer is summarized in Figure 1. Further studies on inhibiting the activations of IL-1β, hence, hold promise for developing a new approach for anti-tumor agents, especially for GI malignancies.

ACKNOWLEDGEMENTS

We would like to thank Prof. John F Smith for editing this manuscript *via* the KKU Publication Clinic, Khon Kaen University, Thailand (PCO-1151).

FOOTNOTES

Author contributions: Khawkhiaw K and Saengboonmee C conceptualized, reviewed, outlined, and wrote the first draft of the manuscript; Panaampon J discussed, edited the manuscript, and created the figure; Imemkamon T discussed and approved the clinical-related context of the manuscript. All authors reviewed and approved the final version of the manuscript.

Supported by National Research Council of Thailand, No. N41A640108; Mekong-Lancang Cooperation Special Fund; The Development and Promotion of Science and Technology Talents Project; and Ministry of Education, Science, Sports, and Culture of Japan, No. 22K16327 and No. 22K08482.

Conflict-of-interest statement: Dr. Saengboonmee reports grants from National Research Council of Thailand, grants from Mekong-Lancang Special Fund, during the conduct of the study.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country of origin: Thailand

ORCID number: Kullanat Khawkhiaw 0009-0006-7922-629X; Jutatip Panaampon 0000-0002-9198-2980; Thanit Imemkamon 0000-0002-5612-2870; Charupong Saengboonmee 0000-0003-1476-1129.

Corresponding Author's Membership in Professional Societies: The Medical Council of Thailand, No. 62243; The Medical Association of Thailand under the Patronage of HM the King, No. 28796.

S-Editor: Fan JR
L-Editor: A
P-Editor: Zheng XM

REFERENCES

1 **Binnewies M**, Roberts EW, Kersten K, Chan V, Fearon DF, Merad M, Coussens LM, Gabrilovich DI, Ostrand-Rosenberg S, Hedrick CC,

Vonderheide RH, Pittet MJ, Jain RK, Zou W, Howcroft TK, Woodhouse EC, Weinberg RA, Krummel MF. Understanding the tumor immune microenvironment (TIME) for effective therapy. *Nat Med* 2018; **24**: 541-550 [PMID: 29686425 DOI: 10.1038/s41591-018-0014-x]
2 **Rébé C**, Ghiringhelli F. Interleukin-1β and Cancer. *Cancers (Basel)* 2020; **12** [PMID: 32635472 DOI: 10.3390/cancers12071791]
3 **Gabay C**, Lamacchia C, Palmer G. IL-1 pathways in inflammation and human diseases. *Nat Rev Rheumatol* 2010; **6**: 232-241 [PMID: 20177398 DOI: 10.1038/nrrheum.2010.4]
4 **Loiarro M**, Ruggiero V, Sette C. Targeting TLR/IL-1R signalling in human diseases. *Mediators Inflamm* 2010; **2010**: 674363 [PMID: 20396389 DOI: 10.1155/2010/674363]
5 **Gelfo V**, Romaniello D, Mazzeschi M, Sgarzi M, Grilli G, Morselli A, Manzan B, Rihawi K, Lauriola M. Roles of IL-1 in Cancer: From Tumor Progression to Resistance to Targeted Therapies. *Int J Mol Sci* 2020; **21** [PMID: 32825489 DOI: 10.3390/ijms21176009]
6 **Zhao R**, Chen X, Ren W, Dai H, Li H, Jia A, Wu Y, Han P, Shao Y. IL-1B rs2853550 polymorphism contributes to esophageal cancer susceptibility in Chinese Han population of Northwest China. *Mol Med* 2020; **26**: 57 [PMID: 32527212 DOI: 10.1186/s10020-020-00178-y]
7 **Chen MF**, Lu MS, Chen PT, Chen WC, Lin PY, Lee KD. Role of interleukin 1 beta in esophageal squamous cell carcinoma. *J Mol Med (Berl)* 2012; **90**: 89-100 [PMID: 21912958 DOI: 10.1007/s00109-011-0809-4]
8 **Chen S**, Shen Z, Liu Z, Gao L, Han Z, Yu S, Kang M. IL-1RA suppresses esophageal cancer cell growth by blocking IL-1α. *J Clin Lab Anal* 2019; **33**: e22903 [PMID: 31102307 DOI: 10.1002/jcla.22903]
9 **Shen Z**, Zhang P, Zhang W, Luo F, Xu H, Chen S, Kang M. IL-1RA inhibits esophageal carcinogenesis and lymphangiogenesis *via* downregulating VEGF-C and MMP9. *Funct Integr Genomics* 2023; **23**: 164 [PMID: 37198330 DOI: 10.1007/s10142-023-01049-5]
10 **Muthupalani S**, Annamalai D, Feng Y, Ganesan SM, Ge Z, Whary MT, Nakagawa H, Rustgi AK, Wang TC, Fox JG. IL-1β transgenic mouse model of inflammation driven esophageal and oral squamous cell carcinoma. *Sci Rep* 2023; **13**: 12732 [PMID: 37543673 DOI: 10.1038/s41598-023-39907-8]
11 **Baumeister T**, Ingermann J, Marcazzan S, Fang HY, Oellinger R, Rad R, Engleitner T, Kleigrewe K, Anand A, Strangmann J, Schmid RM, Wang TC, Quante M. Anti-inflammatory chemoprevention attenuates the phenotype in a mouse model of esophageal adenocarcinoma. *Carcinogenesis* 2021; **42**: 1068-1078 [PMID: 33878160 DOI: 10.1093/carcin/bgab032]
12 **Yin S**, Lan C, Pei H, Zhu Z. Expression of interleukin 1β in gastric cancer tissue and its effects on gastric cancer. *Onco Targets Ther* 2016; **9**: 31-35 [PMID: 26730201 DOI: 10.2147/OTT.S94277]
13 **Xu J**, Yin Z, Cao S, Gao W, Liu L, Yin Y, Liu P, Shu Y. Systematic review and meta-analysis on the association between IL-1B polymorphisms and cancer risk. *PLoS One* 2013; **8**: e63654 [PMID: 23704929 DOI: 10.1371/journal.pone.0063654]
14 **Ren HY**, Huang GL, Liu WM, Zhang W, Liu Y, Su GQ, Shen DY. IL-1β induced RXRα overexpression through activation of NF-κB signaling in gastric carcinoma. *Biomed Pharmacother* 2016; **78**: 329-334 [PMID: 26898458 DOI: 10.1016/j.biopha.2016.01.033]
15 **Yamanaka N**, Morisaki T, Nakashima H, Tasaki A, Kubo M, Kuga H, Nakahara C, Nakamura K, Noshiro H, Yao T, Tsuneyoshi M, Tanaka M, Katano M. Interleukin 1beta enhances invasive ability of gastric carcinoma through nuclear factor-kappaB activation. *Clin Cancer Res* 2004; **10**: 1853-1859 [PMID: 15014040 DOI: 10.1158/1078-0432.ccr-03-0300]
16 **Tu S**, Bhagat G, Cui G, Takaishi S, Kurt-Jones EA, Rickman B, Betz KS, Penz-Oesterreicher M, Bjorkdahl O, Fox JG, Wang TC. Overexpression of interleukin-1beta induces gastric inflammation and cancer and mobilizes myeloid-derived suppressor cells in mice. *Cancer Cell* 2008; **14**: 408-419 [PMID: 18977329 DOI: 10.1016/j.ccr.2008.10.011]
17 **Eum HH**, Kwon M, Ryu D, Jo A, Chung W, Kim N, Hong Y, Son DS, Kim ST, Lee J, Lee HO, Park WY. Tumor-promoting macrophages prevail in malignant ascites of advanced gastric cancer. *Exp Mol Med* 2020; **52**: 1976-1988 [PMID: 33277616 DOI: 10.1038/s12276-020-00538-y]
18 **Gunter MJ**, Canzian F, Landi S, Chanock SJ, Sinha R, Rothman N. Inflammation-related gene polymorphisms and colorectal adenoma. *Cancer Epidemiol Biomarkers Prev* 2006; **15**: 1126-1131 [PMID: 16775170 DOI: 10.1158/1055-9965.EPI-06-0042]
19 **Graziano F**, Ruzzo A, Canestrari E, Loupakis F, Santini D, Rulli E, Humar B, Galluccio N, Bisonni R, Floriani I, Maltese P, Falcone A, Tonini G, Catalano V, Fontana A, Giustini L, Masi G, Vincenzi B, Alessandroni P, Magnani M. Variations in the interleukin-1 receptor antagonist gene impact on survival of patients with advanced colorectal cancer. *Pharmacogenomics J* 2009; **9**: 78-84 [PMID: 19104506 DOI: 10.1038/tpj.2008.16]
20 **Liu L**, Zhai Z, Wang D, Ding Y, Chen X, Wang Q, Shu Z, Wu M, Chen L, He X, Fan D, Pan F, Xing M. The association between IL-1 family gene polymorphisms and colorectal cancer: A meta-analysis. *Gene* 2021; **769**: 145187 [PMID: 32998046 DOI: 10.1016/j.gene.2020.145187]
21 **Liu H**, Zeng J, Huang W, Xu Q, Ye D, Sun R, Zhang D. Colorectal Cancer Is Associated with a Deficiency of Lipoxin A(4), an Endogenous Anti-inflammatory Mediator. *J Cancer* 2019; **10**: 4719-4730 [PMID: 31528237 DOI: 10.7150/jca.32456]
22 **Li Y**, Wang L, Pappan L, Galliher-Beckley A, Shi J. IL-1β promotes stemness and invasiveness of colon cancer cells through Zeb1 activation. *Mol Cancer* 2012; **11**: 87 [PMID: 23174018 DOI: 10.1186/1476-4598-11-87]
23 **Koncina E**, Nurmik M, Pozdeev VI, Gilson C, Tsenkova M, Begaj R, Stang S, Gaigneaux A, Weindorfer C, Rodriguez F, Schmoetten M, Klein E, Karta J, Atanasova VS, Grzyb K, Ullmann P, Halder R, Hengstschläger M, Graas J, Augendre V, Karapetyan YE, Kerger L, Zuegel N, Skupin A, Haan S, Meiser J, Dolznig H, Letellier E. IL1R1(+) cancer-associated fibroblasts drive tumor development and immunosuppression in colorectal cancer. *Nat Commun* 2023; **14**: 4251 [PMID: 37460545 DOI: 10.1038/s41467-023-39953-w]
24 **Hai Ping P**, Feng Bo T, Li L, Nan Hui Y, Hong Z. IL-1β/NF-kb signaling promotes colorectal cancer cell growth through miR-181a/PTEN axis. *Arch Biochem Biophys* 2016; **604**: 20-26 [PMID: 27264420 DOI: 10.1016/j.abb.2016.06.001]
25 **Teimourian S**, Moghanloo E. Role of PTEN in neutrophil extracellular trap formation. *Mol Immunol* 2015; **66**: 319-324 [PMID: 25913476 DOI: 10.1016/j.molimm.2015.03.251]
26 **Eissing M**, Ripken L, Schreibelt G, Westdorp H, Ligtenberg M, Netea-Maier R, Netea MG, de Vries IJM, Hoogerbrugge N. PTEN Hamartoma Tumor Syndrome and Immune Dysregulation. *Transl Oncol* 2019; **12**: 361-367 [PMID: 30504085 DOI: 10.1016/j.tranon.2018.11.003]
27 **Wang G**, Li Y, Wang P, Liang H, Cui M, Zhu M, Guo L, Su Q, Sun Y, McNutt MA, Yin Y. PTEN regulates RPA1 and protects DNA replication forks. *Cell Res* 2015; **25**: 1189-1204 [PMID: 26403191 DOI: 10.1038/cr.2015.115]
28 **Allen IC**, TeKippe EM, Woodford RM, Uronis JM, Holl EK, Rogers AB, Herfarth HH, Jobin C, Ting JP. The NLRP3 inflammasome functions as a negative regulator of tumorigenesis during colitis-associated cancer. *J Exp Med* 2010; **207**: 1045-1056 [PMID: 20385749 DOI: 10.1084/jem.20100050]
29 **Bent R**, Moll L, Grabbe S, Bros M. Interleukin-1 Beta-A Friend or Foe in Malignancies? *Int J Mol Sci* 2018; **19** [PMID: 30042333 DOI: 10.3390/ijms19082155]
30 **Qian H**, Zhang D, Bao C. Two variants of Interleukin-1B gene are associated with the decreased risk, clinical features, and better overall

survival of colorectal cancer: a two-center case-control study. *Aging (Albany NY)* 2018; **10**: 4084-4092 [PMID: 30563955 DOI: 10.18632/aging.101695]

31 **Hirankarn N**, Kimkong I, Kummee P, Tangkijvanich P, Poovorawan Y. Interleukin-1beta gene polymorphism associated with hepatocellular carcinoma in hepatitis B virus infection. *World J Gastroenterol* 2006; **12**: 776-779 [PMID: 16521194 DOI: 10.3748/wjg.v12.i5.776]

32 **Tanaka Y**, Furuta T, Suzuki S, Orito E, Yeo AE, Hirashima N, Sugauchi F, Ueda R, Mizokami M. Impact of interleukin-1beta genetic polymorphisms on the development of hepatitis C virus-related hepatocellular carcinoma in Japan. *J Infect Dis* 2003; **187**: 1822-1825 [PMID: 12751042 DOI: 10.1086/375248]

33 **Liu G**, Sun J, Yang ZF, Zhou C, Zhou PY, Guan RY, Sun BY, Wang ZT, Zhou J, Fan J, Qiu SJ, Yi Y. Cancer-associated fibroblast-derived CXCL11 modulates hepatocellular carcinoma cell migration and tumor metastasis through the circUBAP2/miR-4756/IFIT1/3 axis. *Cell Death Dis* 2021; **12**: 260 [PMID: 33707417 DOI: 10.1038/s41419-021-03545-7]

34 **Zhang C**, Li Q, Xu Q, Dong W, Li C, Deng B, Gong J, Zhang LZ, Jin J. Pulmonary interleukin 1 beta/serum amyloid A3 axis promotes lung metastasis of hepatocellular carcinoma by facilitating the pre-metastatic niche formation. *J Exp Clin Cancer Res* 2023; **42**: 166 [PMID: 37443052 DOI: 10.1186/s13046-023-02748-4]

35 **Faure-Dupuy S**, Delphin M, Aillot L, Dimier L, Lebossé F, Fresquet J, Parent R, Matter MS, Rivoire M, Bendriss-Vermare N, Salvetti A, Heide D, Flores L, Klumpp K, Lam A, Zoulim F, Heikenwälder M, Durantel D, Lucifora J. Hepatitis B virus-induced modulation of liver macrophage function promotes hepatocyte infection. *J Hepatol* 2019; **71**: 1086-1098 [PMID: 31349000 DOI: 10.1016/j.jhep.2019.06.032]

36 **He Q**, Liu M, Huang W, Chen X, Zhang B, Zhang T, Wang Y, Liu D, Xie M, Ji X, Sun M, Tian D, Xia L. IL-1β-Induced Elevation of Solute Carrier Family 7 Member 11 Promotes Hepatocellular Carcinoma Metastasis Through Up-regulating Programmed Death Ligand 1 and Colony-Stimulating Factor 1. *Hepatology* 2021; **74**: 3174-3193 [PMID: 34288020 DOI: 10.1002/hep.32062]

37 **Dang Y**, Chen J, Feng W, Qiao C, Han W, Nie Y, Wu K, Fan D, Xia L. Interleukin 1β-mediated HOXC10 Overexpression Promotes Hepatocellular Carcinoma Metastasis by Upregulating PDPK1 and VASP. *Theranostics* 2020; **10**: 3833-3848 [PMID: 32206125 DOI: 10.7150/thno.41712]

38 **Su B**, Luo T, Zhu J, Fu J, Zhao X, Chen L, Zhang H, Ren Y, Yu L, Yang X, Wu M, Feng G, Li S, Chen Y, Wang H. Interleukin-1β/Iinterleukin-1 receptor-associated kinase 1 inflammatory signaling contributes to persistent Gankyrin activation during hepatocarcinogenesis. *Hepatology* 2015; **61**: 585-597 [PMID: 25294684 DOI: 10.1002/hep.27551]

39 **Takahashi R**, Macchini M, Sunagawa M, Jiang Z, Tanaka T, Valenti G, Renz BW, White RA, Hayakawa Y, Westphalen CB, Tailor Y, Iuga AC, Gonda TA, Genkinger J, Olive KP, Wang TC. Interleukin-1β-induced pancreatitis promotes pancreatic ductal adenocarcinoma *via* B lymphocyte-mediated immune suppression. *Gut* 2021; **70**: 330-341 [PMID: 32393543 DOI: 10.1136/gutjnl-2019-319912]

40 **Caronni N**, La Terza F, Vittoria FM, Barbiera G, Mezzanzanica L, Cuzzola V, Barresi S, Pellegatta M, Canevazzi P, Dunsmore G, Leonardi C, Montaldo E, Lusito E, Dugnani E, Citro A, Ng MSF, Schiavo Lena M, Drago D, Andolfo A, Brugiapaglia S, Scagliotti A, Mortellaro A, Corbo V, Liu Z, Mondino A, Dellabona P, Piemonti L, Taveggia C, Doglioni C, Cappello P, Novelli F, Iannacone M, Ng LG, Ginhoux F, Crippa S, Falconi M, Bonini C, Naldini L, Genua M, Ostuni R. IL-1β(+) macrophages fuel pathogenic inflammation in pancreatic cancer. *Nature* 2023; **623**: 415-422 [PMID: 37914939 DOI: 10.1038/s41586-023-06685-2]

41 **Das S**, Shapiro B, Vucic EA, Vogt S, Bar-Sagi D. Tumor Cell-Derived IL1β Promotes Desmoplasia and Immune Suppression in Pancreatic Cancer. *Cancer Res* 2020; **80**: 1088-1101 [PMID: 31915130 DOI: 10.1158/0008-5472.CAN-19-2080]

42 **Biffi G**, Oni TE, Spielman B, Hao Y, Elyada E, Park Y, Preall J, Tuveson DA. IL1-Induced JAK/STAT Signaling Is Antagonized by TGFβ to Shape CAF Heterogeneity in Pancreatic Ductal Adenocarcinoma. *Cancer Discov* 2019; **9**: 282-301 [PMID: 30366930 DOI: 10.1158/2159-8290.CD-18-0710]

43 **Zhang D**, Li L, Jiang H, Li Q, Wang-Gillam A, Yu J, Head R, Liu J, Ruzinova MB, Lim KH. Tumor-Stroma IL1β-IRAK4 Feedforward Circuitry Drives Tumor Fibrosis, Chemoresistance, and Poor Prognosis in Pancreatic Cancer. *Cancer Res* 2018; **78**: 1700-1712 [PMID: 29363544 DOI: 10.1158/0008-5472.CAN-17-1366]

44 **Chaturmohta A**, Dixit R, Narayan G, Gupta P, Prasad SB, Yadav S, Shukla VK. Do Expression Profiles of Cytokines VEGF, TNF- α, IL-1β, IL-6 and IL-8 Correlate with Gallbladder Cancer? *J Cancer Sci Clin Oncol* 2015; **2**: 202 [DOI: 10.15744/2394-6520.2.202]

45 **Patil RS**, Shah SU, Shrikhande SV, Goel M, Dikshit RP, Chiplunkar SV. IL17 producing γδT cells induce angiogenesis and are associated with poor survival in gallbladder cancer patients. *Int J Cancer* 2016; **139**: 869-881 [PMID: 27062572 DOI: 10.1002/ijc.30134]

46 **Vishnoi M**, Pandey SN, Choudhuri G, Mittal B. IL-1 gene polymorphisms and genetic susceptibility of gallbladder cancer in a north Indian population. *Cancer Genet Cytogenet* 2008; **186**: 63-68 [PMID: 18940468 DOI: 10.1016/j.cancergencyto.2008.05.004]

47 **Guo R**, Qin Y, Shi P, Xie J, Chou M, Chen Y. IL-1β promotes proliferation and migration of gallbladder cancer cells *via* Twist activation. *Oncol Lett* 2016; **12**: 4749-4755 [PMID: 28105184 DOI: 10.3892/ol.2016.5254]

48 **Lurje I**, Gaisa NT, Dahl E, Knüchel R, Strnad P, Trautwein C, Tacke F, Neumann UP, Czigany Z, Lurje G. Genetic polymorphisms in interleukin-1β (rs1143634) and interleukin-8 (rs4073) are associated with survival after resection of intrahepatic cholangiocarcinoma. *Sci Rep* 2023; **13**: 12283 [PMID: 37507547 DOI: 10.1038/s41598-023-39487-7]

49 **Song J**, Li Y, Bowlus CL, Yang G, Leung PSC, Gershwin ME. Cholangiocarcinoma in Patients with Primary Sclerosing Cholangitis (PSC): a Comprehensive Review. *Clin Rev Allergy Immunol* 2020; **58**: 134-149 [PMID: 31463807 DOI: 10.1007/s12016-019-08764-7]

50 **Kunzmann LK**, Schoknecht T, Poch T, Henze L, Stein S, Kriz M, Grewe I, Preti M, Hartl J, Pannicke N, Peiseler M, Sebode M, Zenouzi R, Horvatits T, Böttcher M, Petersen BS, Weiler-Normann C, Hess LU, Ahrenstorf AE, Lunemann S, Martrus G, Fischer L, Li J, Carambia A, Kluwe J, Huber S, Lohse AW, Franke A, Herkel J, Schramm C, Schwinge D. Monocytes as Potential Mediators of Pathogen-Induced T-Helper 17 Differentiation in Patients With Primary Sclerosing Cholangitis (PSC). *Hepatology* 2020; **72**: 1310-1326 [PMID: 33090557 DOI: 10.1002/hep.31140]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com

© 2024 Baishideng Publishing Group Inc. All rights reserved.