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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*.

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EDITORIAL

Immune-related gene characteristics: A new chapter in precision treatment of gastric cancer

Lei Gao, Qiang Lin

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Lei Gao, Department of Medical Imaging, North China Petroleum Bureau General Hospital, Hebei Medical University, Renqiu 062552, Hebei Province, China

Qiang Lin, Department of Oncology, North China Petroleum Bureau General Hospital, Hebei Medical University, Renqiu 062552, Hebei Province, China

Corresponding author: Qiang Lin, MD, PhD, Professor, Department of Oncology, North China Petroleum Bureau General Hospital, Hebei Medical University, No. 8 Huizhan Avenue, Renqiu 062552, Hebei Province, China. billhappy001@163.com

Abstract

Gastric cancer ranks as the sixth most prevalent cancer worldwide. In recent research within the realm of gastric cancer treatment, the identification and application of immune-related genetic features have emerged as groundbreaking advancements. The study by Ma *et al*, which developed a prognostic model based on 10 genes, categorizes patients into high and low-risk groups to predict their responsiveness to immune checkpoint inhibitor therapy. This research underscores the potential of immune-related genes as biomarkers for personalized treatment, offering insights into tumor mutation burden and immune phenotype scores. We advocate for further validation, understanding of biological mechanisms, and integration of diverse datasets to enhance the model's predictive accuracy and clinical application, marking a significant step towards personalized and precise treatment for gastric cancer.

Key Words: Gastric cancer; Personalized treatment; Immune-related genes; Immunotherapy; Genomics

Core Tip: In the study conducted by Ma *et al*, a prognostic model for gastric cancer was developed, leveraging 10 pivotal immune-related genes to differentiate patients into high and low-risk categories. This model aims to refine immunotherapy strategies, enhancing the personalization and precision of treatments. Such discoveries hold the promise of introducing novel biomarkers for the personalized medical treatment and immunotherapy of gastric cancer, underscoring the critical importance of further research and validation.

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INTRODUCTION

Gastric cancer, which represents a formidable threat to global health, is associated with persistently high incidence and mortality rates[1]. Statistics from the World Health Organization, it ranks as the sixth most common cancer worldwide, with over a million new cases, and ranking fifth in terms of cancer-related deaths[2]. Its geographical distribution exhibits pronounced regional characteristics, with significantly higher incidence rates in East Asia, Eastern Europe, and parts of South America compared with other regions[3]. The high-risk areas for gastric cancer are often associated with dietary habits, environmental factors, and Helicobacter pylori infection. The primary therapeutic strategies for gastric cancer include surgical resection, chemotherapy, radiotherapy, targeted therapy, and immunotherapy[4]. Surgical resection offers a potential cure for early-stage gastric cancer and some locally advanced cases, while chemotherapy and radiotherapy are mainstream treatments for late-stage patients. In recent years, targeted and immunotherapies have emerged as research and clinical trial focal points, offering new hope for effective gastric cancer treatment[5]. Nevertheless, the overall five-year survival rate for gastric cancer patients remains low, with persistent challenges in enhancing treatment efficacy and patient quality of life.

IMMUNE-RELATED GENE CHARACTERISTICS IN GASTRIC CANCER

Recent studies in the field of gastric cancer treatment have marked a breakthrough with identification and application of immune-related gene characteristics. Studies have elucidated the characteristics of a series of genes that play crucial roles in the immune response against tumors. Through in-depth analysis of genetic information derived from analysis of in patients' tumor tissues, researchers can now predict the immune microenvironment and response status of gastric cancer, offering customized treatment guidance. For instance, the expression patterns of specific immune-related genes have been shown to indicate patient responsiveness to immune checkpoint inhibitor therapy[6].

Ma *et al*[7] analyzed differentially expressed immune-related genes (DEIRGs) in gastric cancer patients and constructed a novel prognostic model based on 10 genes, of which 9 were risk genes and one was a protective gene. Patients were stratified into high-risk and low-risk groups based on median risk scores. The study found that low-risk group patients had higher tumor mutation burden and immune phenotype scores, potentially indicating better responsiveness to immune checkpoint inhibitor therapy. Further comparison of immune cell infiltration between high-risk and low-risk groups revealed differences in immune response, providing new personalized treatment biomarkers and directions for the treatment of gastric cancer patients. The population was divided into training and testing cohorts for internal validation, with Kaplan Meier survival rate, receiver operating characteristic, and risk curve analyses indicating the risk model's good predictive capability of the risk model. The identified immune-related genes have also been partially confirmed to be associated with tumor occurrence and progression. Increasing evidence suggests the significant role of TMSB15A in tumor progression, with its upregulation in various cancer cell lines linked to cell migration and proliferation. TMSB15A mRNA levels have been identified as a reliable predictor for triple-negative breast cancer[8]. GLP2R has been associated with gastrointestinal tumors, with its knockdown significantly inhibiting gastric cancer (GC) cell proliferation and migration[9,10]. Silencing of LGR6, which is expressed at high levels in GC cell lines and gastric adenocarcinoma tissues, has been shown to suppress cell proliferation and migration, along with the expression of MMP-9, β-catenin, CCNA2, CDK-2, and ERK1/2 when silenced[11].

FUTURE DIRECTIONS IN RESEARCH

In light of these findings, the integration of external independent datasets into the existing model is recommended to enhance its generalizability. Further exploration of the biological mechanisms of DEIRGs in gastric cancer, including their impact on patient immune response and treatment outcomes, is crucial. The inclusion of data from diverse populations and treatment backgrounds will improve the model's diversity and adaptability. Long-term follow-ups and prospective clinical trials could further validate the model's predictive accuracy and test its clinical application value, improving the

comprehensiveness of the research and providing stronger support for the development of personalized treatment for gastric cancer patients.

The discovery of immune-related gene characteristics undoubtedly heralds a new chapter in the treatment of gastric cancer. Personalized medicine, particularly in the field of oncology, is increasingly becoming a key approach to enhancing treatment efficacy and reducing unnecessary drug side effects. By providing information regarding the activity and regulatory patterns of immune cells in the patient's tumor microenvironment, immune-related gene characteristics can help physicians determine patient responsiveness to immunotherapy, achieving precise and individualized treatment. For patients likely to respond well to immunotherapy, the application of these biomarkers can significantly improve treatment outcomes and survival rates[12]. Furthermore, at the drug development level, immune-related gene characteristics provide a basis for identifying new immunotherapy targets, propelling the research and development of a new generation of immunotherapeutic drugs.

Although immunotherapy based on the PD-1/PD-L1 axis has established its place in gastric cancer treatment, not all patients benefit from it. Research on immune-related gene characteristics helps identify patient groups likely to benefit from immunotherapy and may reveal the molecular mechanisms underlying some patients' resistance to treatment[13]. Through such insights, researchers and physicians can design more precise treatment plans, tailoring therapies to individual patients. Thus, the significance of immune-related gene characteristics in gastric cancer treatment extends beyond mere biomarkers; paving the way for true precision medicine and advancing the innovation of gastric cancer immunotherapy.

Ensuring the stability and reproducibility of the application of immune-related gene characteristics in clinical gastric cancer treatment poses a significant challenge. Achieving this goal requires large-scale, multi-center studies to validate these gene characteristics' reliability across different populations and geographical regions[14]. Additionally, the heterogeneity of gene expression may affect the accuracy of characteristics, necessitating further research into effectively capturing and analyzing subtle changes in the tumor's immune microenvironment.

Future research directions should include a deeper investigation into the practical value of immune-related gene characteristics in treatment decisions, such as in guiding personalized treatment plans through predicting treatment response and resistance. Incorporating multi-omics data, such as genomic, proteomic, and metabolomic data, could enhance the accuracy with which gene characteristics can be utilized to predict treatment efficacy and prognosis[15].

CONCLUSION

To validate the clinical application value of gene characteristics, not only should their impact on treatment decisions be assessed through prospective and retrospective studies; furthermore, randomized controlled clinical trials should also be conducted to test whether treatment strategies based on gene characteristics can offer better outcomes than current standard treatments. Considering the economic cost of treatments, health economics assessments are indispensable, helping to determine the feasibility of integrating immune-related gene characteristics into clinical practice. Through such comprehensive analyses, applications based on immune-related gene characteristics can be anticipated to play a key role in gastric cancer treatment in the future. As research on immune-related gene characteristics advances, the field of gastric cancer treatment stands at a new clinical translational threshold. Transforming laboratory research findings into clinical treatment strategies requires close collaboration between the scientific community and clinicians. Such interdisciplinary teamwork not only accelerates the birth of new treatment strategies but also ensures their practicality and effectiveness. Researchers, being well-versed in tumor immunology and gene characteristics, drive the advancement of gastric cancer treatment with their innovative studies. However, clinicians play a crucial role in the actual application of these treatment methods. They are in direct contact with patients, deeply understanding disease characteristics, treatment responses, and clinical needs. Through collaboration, not only can the clinical efficacy of new treatment methods be more accurately assessed, but potential issues in practical application, such as individualized treatment adjustments, side effect management, and cost-effectiveness evaluation, can also be identified and addressed. Therefore, with the common goal of advancing gastric cancer treatment, the scientific community and clinicians need to strengthen communication and establish a more integrated and efficient cooperation mechanism. This includes, but is not limited to, joint involvement in clinical trial design, data sharing, result interpretation, and the promotion and implementation of new treatment strategies. Additionally, collaboration should extend to the education and training domain, ensuring that the latest research findings are disseminated among doctors and applied in clinical practice. In this context, we call on healthcare system managers, relevant scientific project funding agencies, and medical insurance policy makers to support this interdisciplinary cooperation in order to provide the necessary resources and policy backing. Only through such support can the clinical translation of scientific achievements be truly realized, continuously improving the diagnosis and treatment of gastric cancer, ultimately enhancing patient survival rates and quality of life.

FOOTNOTES

Author contributions: Gao L and Lin Q contributed to this paper; Lin Q designed the overall concept and outline of the manuscript; Gao L wrote the draft of the manuscript; Gao L and Lin Q contributed to the writing and editing the manuscript.

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Country of origin: China

ORCID number: Lei Gao 0000-0002-3388-4901; Qiang Lin 0000-0001-9599-4121.

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