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Editorial Board of World Journal of Gastrointestinal Oncology, Salem Youssef Mohamed, MD, Professor, Gastroenterology and Hepatology Unit, Department of Internal Medicine, Zagazig University, Zagazig 44516, Egypt. salemyousefmohamed@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 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for WJGO as 2.5; JIF without journal self cites: 2.5; 5-year JIF: 2.8; JIF Rank: 71/143 in gastroenterology and hepatology; JIF Quartile: Q2; and 5-year JIF Quartile: Q2. The WJGO’s CiteScore for 2023 is 4.2 and Scopus CiteScore rank 2023: Gastroenterology is 80/167; Oncology is 196/404.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Si Zhao; Production Department Director: Xiang Li; Cover Editor: Jia-Ru Fan.
Research status and hotspots of tight junctions and colorectal cancer: A bibliometric and visualization analysis

Hui-Min Li, Yin Liu, Meng-Di Hao, Xiao-Qing Liang, Da-Jin Yuan, Wen-Bin Huang, Wen-Jie Li, Lei Ding

Abstract

BACKGROUND
Colorectal cancer (CRC) is the third most common cancer worldwide and the second leading cause of cancer-related death. Over the past two decades, numerous researchers have provided important evidence regarding the role of tight junction (TJ) proteins in the occurrence and progression of CRC. The causal relationship between the presence of specific TJ proteins and the development of CRC has also been confirmed. Despite the large number of publications in this field, a bibliometric study to review the current state of research and highlight the research trends and hotspots in this field has not yet been performed.

AIM
To analyze research on TJs and CRC, summarize the field’s history and current status, and predict future research directions.

METHODS
We searched the Science Citation Index Expanded database for all literature on CRC and TJs from 2001-2023. We used bibliometrics to analyze the data of these papers, such as the authors, countries, institutions, and references. Co-authorship, co-citation, and co-occurrence analyses were the main methods of analysis. CiteSpace and VOSviewer were used to visualize the results.

RESULTS
A total of 205 studies were ultimately identified. The number of publications on this topic has steadily increased since 2007. China and the United States have made the largest contributions to this field. Anticancer Research was the most prolific journal, publishing 8 articles, while the journal Oncogene had the highest average citation rate (68.33). Professor Dhawan P was the most prolific and cited author in this field. Co-occurrence analysis of keywords revealed that “tight junction protein expression”, “colorectal cancer”, “intestinal microbiota”, and “inflammatory bowel disease” had the highest frequency of occurrence, revealing...
the research hotspots and trends in this field.

CONCLUSION
This bibliometric analysis evaluated the scope and trends of TJ proteins in CRC, providing valuable research perspectives and future directions for studying the connection between the two. It is recommended to focus on emerging research hotspots, such as the correlations among intestinal microbiota, inflammatory bowel disease, TJ protein expression, and CRC.

Key Words: Colorectal cancer; Tight junctions; Bibliometric analysis; Research trends; Hot spots

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Core Tip: This bibliometric analysis evaluated the scope and trends of tight junction (TJ) proteins in colorectal cancer (CRC), providing valuable research perspectives and future directions for studying the connection between the two. It is recommended to focus on emerging hotspots such as the correlations among intestinal microbiota, inflammatory bowel disease, TJ protein expression, and CRC.

INTRODUCTION
Globally, colorectal cancer (CRC) holds the position of the third most prevalent cancer and is the second top contributor to cancer-related deaths. The year 2018 saw global estimates suggesting around 1.8 million new cases and 881000 fatalities [1]. With its continued rise in Western countries, it is projected that by 2030, the global incidence of CRC will increase to 2.2 million new cases and 1.1 million deaths[2]. In China, it is estimated that there are more than 376000 new cases and 191000 deaths annually[3]. Despite regional variations and declining trends, the burden of CRC remains high due to population growth. Environmental factors such as obesity, Western dietary habits, smoking, and alcohol consumption are associated with CRC[4]. Additionally, genetic mutations and epigenetic changes are known to be involved in the occurrence and progression of CRC[5,6]. There is increasing evidence indicating a close association between tight junction (TJ) protein expression and CRC[7,8].

TJs are crucial intercellular connections essential for building epithelial barriers and maintaining epithelial polarity[9]. They regulate tissue homeostasis and integrity by controlling paracellular permeability and polarity. Beyond the static expression that promotes barrier function, TJs dynamically participate in regulating a range of cellular processes, including proliferation, migration, plasticity, and differentiation, all of which are central to cancer initiation and progression[10]. Numerous studies have confirmed that disrupting TJ integrity leads to cell invasion and proliferation and, consequently, the development of CRC and even distant metastasis[11-13].

Current research has focused on various members of the claudin family, elucidating their roles in CRC development. Cldn-2 is upregulated in CRC patients and is associated with poor survival. Depletion of Cldn-2 has been shown to be associated with CRC stem-like renewal[14]. Abnormal expression and distribution of claudin-7, a key protein in epithelial cells, have been reported in various human malignancies, including lung, colon, ovarian, breast, gastric, esophageal, and prostate cancers, and are associated with cancer progression and metastasis[15]. Claudin-7 interacts with integrin β1 to inhibit CRC cell proliferation and migration[16]. These studies collectively demonstrate the intimate relationship between TJ proteins and the metastasis of CRC, suggesting their potential as novel targets for CRC therapy.

Utilizing public literature sources like the Web of Science, bibliometric analysis, a statistical technique, is employed to examine and depict trends in research[18]. It’s now a prevalent approach for evaluating the reliability, caliber, and influence of scholarly endeavors[19,20]. In recent years, an increasing number of studies have focused on TJ proteins and CRC. However, systematic research on the relationship between TJ proteins and CRC through bibliometric analysis has yet to be conducted. Through bibliometric analysis, researchers can better understand the current status, trends, and hotspots in this field. This study aimed to reveal new trends in TJ protein and CRC research, such as articles, journals, and cooperation patterns among key authors and institutions, and explore the research hotspots and future directions in the field through bibliometric analysis.
MATERIALS AND METHODS

Search strategy
This study utilized the Web of Science as the data source. All potentially relevant publications were collected based on the topic (TS) using the following search strategy: #1: [TS = (colorectal* OR colon* OR rectum* OR rectal*)] #2: TS = (cancer* OR neoplasm* OR carcinoma* OR adenoma*) #3: TS = (claudins* OR CLDNs* OR claudin* OR CLDN*). Final dataset: #1 AND #2 AND #3. To capture as many data sources as possible, wildcards were used, which can substitute for any other character and allow keywords to have variable endings. For example, “cancer” would return both “cancer” and “cancers”. English articles published from January 1, 2001, to December 31, 2023, were retrieved.

Study selection
Figure 1 depicts the criteria for selection and the process of reviewing literature for this research. Concisely, our initial search involved entering search terms, followed by a review by two researchers of the identified publications, discarding those failing to satisfy the specified inclusion criteria: (1) Publications were limited to the English language only; (2) Document types included articles and reviews, excluding letters, comments, and conference abstracts; (3) Publications were sourced from the Science Citation Index Expanded database; (4) The search timeframe was from January 1, 2001, to December 31, 2023, spanning 23 years; (5) Publications focused on patients with CRC (including patients with CRC, preoperative and postoperative patients with CRC), CRC animal models, and CRC cell models and evaluated the relevance of the study subjects to intestinal TJ proteins; and (6) To avoid bias due to daily updates of the database, searches and screening of publications were conducted and completed on the same day.

Data extraction
Two researchers independently reviewed all included publications, downloaded them, and exported them into different file formats for analysis. The following indicators were extracted: The number of publications, citation frequency, countries, institutions, journals, authors, keywords, and the journal’s impact factor for the year 2023.

RESULTS

Global publication and collaboration trends
From January 1, 2001, to December 31, 2023, a total of 677 records were identified. Altogether, 239 records were omitted due to their nature as conference abstracts, letters, and continuous papers. An additional evaluation of the 438 remaining records was conducted either by reading abstracts or full texts. In the end, the bibliometric analysis incorporated 205 studies that satisfied both the inclusion and exclusion requirements (Figure 1). These papers were published by 1337 authors from 355 institutions in 32 countries and appeared in 127 journals. These articles cited 7060 references from 1361 journals. The number of annual and cumulative publications has significantly increased over the past 23 years. The peak number of papers was published in 2023 (24 papers) (Figure 2).

Country/region analysis
A total of 32 countries/regions have published research on TJ proteins and CRC. Table 1 shows the five most productive countries. China had the highest number of publications, with 66 papers, followed by the United States (46 papers) and Japan (30 papers). The United States had the highest citation rate (3227 times), followed by Japan (1186 times) and China (994 times). Germany (74 times) and the United States (70.15 times) had the highest average citation rates.

The collaboration network among these countries is shown in Figure 3A. All countries contributed at least 3 publications in this field, with 10 countries represented in the network map. Figure 3B also illustrates the years of collaboration among countries, showing that China and the United States can be considered the central countries in the network and have had the closest mutual connections in recent years. Furthermore, the United States has connections with almost all countries in the network, with particularly close ties to Japan, South Korea, Canada, and Spain. Compared to the United States, China has fewer connections with other countries, with some connections to countries such as Japan and Germany.

Authors and journals
Additionally, we evaluated the most productive authors of the articles included in this study. Professor Dhawan P published the most papers, with a total of 17, followed by Singh AB (15 papers) and Ding Lei (9 papers). Similarly, Professor Dhawan P had the highest total number of citations (922), while Professor Sharma A had the highest average number of citations (83.6) (Table 2).

Next, the researchers analyzed the journals in which the articles were published from 2001 to 2023. A total of 127 journals published articles in this field, with the 9 journals with the greatest publication frequency listed in Table 3. The top three journals were Anticancer Research (8, 3.90%), International Journal of Molecular Sciences (7, 3.41%), and Oncogene (6, 2.92%). Among the top 9 journals, Oncogene had the greatest number of citations, with 410 citations and an average citation rate of 68.33, making it an influential journal in this field.

Co-citation analysis
Co-citation analysis refers to the relationship between two (or more) papers that are simultaneously cited by one or more subsequent papers, forming a co-citation relationship[1]. This research method is used to measure the degree of...
### Table 1 Five most productive countries/regions for research related to tight junctions in colorectal cancer

<table>
<thead>
<tr>
<th>Countries/regions</th>
<th>Publications</th>
<th>Citations</th>
<th>Citations per-publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>66</td>
<td>994</td>
<td>15.06</td>
</tr>
<tr>
<td>United States</td>
<td>46</td>
<td>3227</td>
<td>70.15</td>
</tr>
<tr>
<td>Japan</td>
<td>30</td>
<td>1186</td>
<td>39.53</td>
</tr>
<tr>
<td>South Korea</td>
<td>13</td>
<td>184</td>
<td>14.15</td>
</tr>
<tr>
<td>Germany</td>
<td>11</td>
<td>814</td>
<td>74.00</td>
</tr>
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### Table 2 Top 12 authors by publications

<table>
<thead>
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<th>Citations</th>
<th>Citations per-publication</th>
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<tr>
<td>Dhawan P</td>
<td>17</td>
<td>922</td>
<td>54.2</td>
</tr>
<tr>
<td>Singh AB</td>
<td>15</td>
<td>708</td>
<td>47.2</td>
</tr>
<tr>
<td>Ding Lei</td>
<td>9</td>
<td>137</td>
<td>15.2</td>
</tr>
<tr>
<td>Wang Kun</td>
<td>8</td>
<td>117</td>
<td>14.6</td>
</tr>
<tr>
<td>Xu Chang</td>
<td>8</td>
<td>117</td>
<td>14.6</td>
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<td>Washington MK</td>
<td>6</td>
<td>423</td>
<td>70.5</td>
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<td>Bhat AA</td>
<td>6</td>
<td>407</td>
<td>67.8</td>
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<td>Ahmad R</td>
<td>6</td>
<td>303</td>
<td>50.5</td>
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<td>Kinugasa T</td>
<td>6</td>
<td>239</td>
<td>39.8</td>
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<td>Sharma A</td>
<td>5</td>
<td>418</td>
<td>83.6</td>
</tr>
<tr>
<td>Krishnan M</td>
<td>5</td>
<td>388</td>
<td>77.6</td>
</tr>
<tr>
<td>Li Wenjing</td>
<td>5</td>
<td>83</td>
<td>16.6</td>
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</table>

### Table 3 Top 9 leading journals in the field of tight junctions and colorectal cancer research from 2001-2023

<table>
<thead>
<tr>
<th>Journal</th>
<th>Publications</th>
<th>Citations</th>
<th>Citations per-publication</th>
<th>Journal IF (2023)</th>
<th>JCR</th>
</tr>
</thead>
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<tr>
<td>Anticancer Research</td>
<td>8</td>
<td>315</td>
<td>39.38</td>
<td>2.0</td>
<td>Q4</td>
</tr>
<tr>
<td>International Journal of Molecular Sciences</td>
<td>7</td>
<td>135</td>
<td>22.14</td>
<td>5.6</td>
<td>Q1</td>
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<tr>
<td>Oncogene</td>
<td>6</td>
<td>410</td>
<td>68.33</td>
<td>8.0</td>
<td>Q1</td>
</tr>
<tr>
<td>Cancer Research</td>
<td>6</td>
<td>337</td>
<td>56.17</td>
<td>11.2</td>
<td>Q1</td>
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<tr>
<td>PLoS One</td>
<td>6</td>
<td>241</td>
<td>40.17</td>
<td>3.7</td>
<td>Q2</td>
</tr>
<tr>
<td>Oncology Reports</td>
<td>5</td>
<td>134</td>
<td>26.80</td>
<td>4.2</td>
<td>Q2</td>
</tr>
<tr>
<td>Cancer Management and Research</td>
<td>4</td>
<td>75</td>
<td>18.75</td>
<td>3.3</td>
<td>Q3</td>
</tr>
<tr>
<td>Biochemical and Biophysical Research Communications</td>
<td>4</td>
<td>88</td>
<td>22.00</td>
<td>3.1</td>
<td>Q2</td>
</tr>
<tr>
<td>Carcinogenesis</td>
<td>4</td>
<td>114</td>
<td>28.50</td>
<td>4.7</td>
<td>Q2</td>
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</tbody>
</table>

The focus was divided into two main clusters, represented in green and red. Table 4 lists the top 6 research articles cited from 2001 to 2023 (data from the Web of Science database). The most cited article was “Claudin-1 regulates cellular transformation and metastatic behavior in colon cancer”, authored by Dhawan P, with 86 citations; this article focused on the expression and role of claudin-1 in colorectal carcinoma and metastasis. The next most cited articles were authored by Miwa N and Resnick MB and were cited 48 and 35 times, respectively. Analysis revealed that these six articles focused mainly on the expression of claudin-1 in CRC and its role in the development of CRC. Additionally, the expression and function of claudin-1 and claudin-7 in breast cancer were analyzed.
Table 4 Top 6 references with the most citations

<table>
<thead>
<tr>
<th>Title</th>
<th>Citations of Web of Science</th>
<th>Author</th>
<th>Country</th>
<th>Journal</th>
<th>IF (2023)</th>
<th>JCR</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claudin-1 regulates cellular transformation and metastatic behavior in colon cancer</td>
<td>86</td>
<td>Dhawan P</td>
<td>United States</td>
<td>The Journal of Clinical Investigation</td>
<td>15.9</td>
<td>Q1</td>
<td>2005</td>
</tr>
<tr>
<td>Involvement of Claudin-1 in the beta-catenin/Tcf signaling pathway and its frequent upregulation in human colorectal cancers</td>
<td>48</td>
<td>Miwa N</td>
<td>United States</td>
<td>Oncology Research</td>
<td>3.1</td>
<td>Q3</td>
<td>2001</td>
</tr>
<tr>
<td>Claudin-1 is a strong prognostic indicator in stage II colonic cancer: a tissue microarray study</td>
<td>35</td>
<td>Resnick MB</td>
<td>United Kingdom</td>
<td>Modern Pathology</td>
<td>7.5</td>
<td>Q1</td>
<td>2005</td>
</tr>
<tr>
<td>Multifunctional strands in tight junctions</td>
<td>35</td>
<td>Tsukita S</td>
<td>United Kingdom</td>
<td>Nature Reviews. Molecular Cell Biology</td>
<td>112.7</td>
<td>Q1</td>
<td>2001</td>
</tr>
<tr>
<td>Loss of the tight junction protein Claudin-7 correlates with histological grade in both ductal carcinoma in situ and invasive ductal carcinoma of the breast</td>
<td>32</td>
<td>Kominsky SL</td>
<td>United Kingdom</td>
<td>Oncogene</td>
<td>8</td>
<td>Q1</td>
<td>2003</td>
</tr>
<tr>
<td>Claudin-2 expression increases tumorigenicity of colon cancer cells: role of epidermal growth factor receptor activation</td>
<td>31</td>
<td>Dhawan P</td>
<td>United Kingdom</td>
<td>Oncogene</td>
<td>8</td>
<td>Q1</td>
<td>2011</td>
</tr>
</tbody>
</table>

Figure 1 The flowchart of the literature screening process. SCI: Science Citation Index; TJ: Tight junction.

Together, all the papers cited references from 1361 journals. We visualized the journals cited more than 50 times using VOSviewer, obtaining a co-citation network of cited journals (Figure 4B). Table 5 lists the 6 journals cited most frequently from 2001 to 2023 (data from the Web of Science database). The top three journals were Cancer Research (377 times), Oncogene (319 times), and Gastroenterology (285 times). The cited journals are represented by clusters of three different colors. The green cluster primarily consisted of basic journals such as Cell Biology and Molecular Biology. References to these journals were made to analyze recent research outcomes and offer theoretical backing for their investigations. Clinical journals focusing on gastrointestinal tumors formed the blue and red groupings.

Keyword visualization

The purpose of keyword co-occurrence analysis was to study the co-occurrence relationships between keywords in a set of publications, reflecting popular topics. A total of 205 research articles that met the inclusion and exclusion criteria were exported from the Web of Science database in pure text format, and keyword analysis was performed using VOSviewer, with a threshold set to 10. Combining some frequently recurring keywords and synonyms, a total of 47 keywords were identified. Figure 5A and B show that “expression” and “colorectal cancer” were the most prominent keywords. All identified keywords could be divided into 3 clusters, represented in red, green, and blue. These clusters represent the most prominent themes in this research field to date.

Figure 5C displays the average year of the appearance of keywords. The use of keywords such as “migration”, “apoptosis”, and “inflammatory bowel disease” has increased in recent years. Recent research has focused on the mechanisms of migration and apoptosis related to TJ proteins and their roles in the development of inflammatory bowel
### Table 5 Top 10 journals with the most citations

<table>
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<th>Citations of Web of Science</th>
<th>Journal IF (2023)</th>
<th>JCR</th>
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<tbody>
<tr>
<td>Cancer Research</td>
<td>377</td>
<td>11.2</td>
<td>Q1</td>
</tr>
<tr>
<td>Oncogene</td>
<td>319</td>
<td>8.0</td>
<td>Q1</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>285</td>
<td>29.4</td>
<td>Q1</td>
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<tr>
<td>Journal of Biological Chemistry</td>
<td>238</td>
<td>4.8</td>
<td>Q2</td>
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<td>Journal of Cell Biology</td>
<td>203</td>
<td>7.8</td>
<td>Q1</td>
</tr>
<tr>
<td>PLoS One</td>
<td>162</td>
<td>3.7</td>
<td>Q2</td>
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<td>Proceedings of the National Academy of Sciences of the United States of America</td>
<td>160</td>
<td>11.1</td>
<td>Q1</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>153</td>
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<td>Q1</td>
</tr>
<tr>
<td>Journal of Clinical Investigation</td>
<td>145</td>
<td>15.9</td>
<td>Q1</td>
</tr>
<tr>
<td>Anticancer Research</td>
<td>140</td>
<td>2.0</td>
<td>Q4</td>
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</table>

**Figure 2** Global number of publications in the field of tight junctions and colorectal cancer from 2001 to 2023. A: The global annual number of published articles; B: The global number of annual cumulative published articles.

**Figure 3** The cooperation network of countries/regions in the field. A: Dots represent countries, with larger dots indicating a greater number of publications. Clusters are marked using different colors, and links represent cooperation between countries; B: The cooperation network of countries/regions in the field. The colors represent the average years.

disease.

Keyword clusters consist of one or more keywords that have specific relationships with each other. Cluster analysis of keywords was performed using CiteSpace software, and Figure 5D shows a Q value of 0.6723 (> 0.3) and an S value of 0.8887 (> 0.7) are displayed, suggesting the clustering outcomes are both strong and plausible[21]. There were a total of 10 clustering patterns, 7 of which were selected for analysis. The cluster keywords included “microbiome” (Cluster 0),
“progression” (Cluster 1), “cell adhesion molecules” (Cluster 2), “\textit{Clostridium perfringens} enterotoxin” (Cluster 3), “prognosis” (Cluster 4), “epithelial–mesenchymal transition” (Cluster 5), and “colorectal cancer” (Cluster 6). There are many connections between the nodes of these clusters, indicating a high degree of keyword co-occurrence in this field.

Keyword timeline visualization was used to display the classification and publication time of the keywords (Figure 6A). Most of the keywords appeared after 2005, with increasing focus on “activation”, “invasion”, “metastasis”, and “gene expression” in recent years. Additionally, this figure visualizes the publication times of the clusters and the relationships between different clusters. Cluster analysis in this research revealed that the predominant areas of interest in this domain are primarily the intestinal microbiota, cell adhesion molecules, prognosis, and epithelial-mesenchymal transition.

If certain keywords are concentrated in a particular period, they are called burst keywords. Burst keywords can reflect different stages of development in a field. CiteSpace was used to detect burst keywords to identify research frontiers in this field, with blue bands indicating the start and end times of the appearance of the word and red bands indicating the start and end years of the burst. The five most common groundbreaking keywords extracted from CRC- and TJ-related papers via CiteSpace are shown in Figure 6B. The keyword with the highest burst intensity was “inflammatory bowel disease” (burst intensity of 4.86), which has been a research hotspot in recent years. This keyword first appeared in 2010 and showed explosive growth in 2021, indicating that an increasing number of studies in recent years have focused on exploring the role of TJ proteins in the process of inflammation-induced carcinogenesis.

**DISCUSSION**

Studies have shown a close association between intestinal TJ proteins and CRC, leading to an increasing number of studies over the past two decades exploring the role of TJs in the occurrence and development of CRC\cite{22-25}. Bibliometrics was used to analyze authors, institutions, countries, and references in the Science Citation Index Expanded literature database to understand research areas; trends were visualized using CiteSpace and VOSviewer. This research method provides a more comprehensive analysis of the literature and produces more intuitive results than conventional systematic reviews. To date, no bibliometric analysis has specifically focused on the relationship between TJ proteins and CRC. Therefore, for the first time, this study used bibliometrics to explore the applications and developments in this field from 2001 to 2023 and speculated on future research trends.

In this bibliometric analysis, we found an increase in the number of annual publications over the past 23 years. This trend indicates growing interest among researchers worldwide in this field. Until 2006, the number of publications related to CRC and TJ proteins increased slowly, followed by a significant increase in related publications after 2007, particularly in recent years (Figure 2). This phenomenon suggests recent rapid development in this field.

We analyzed the most influential countries, authors, and journals in this field. The top three countries accounted for approximately 60% of all publications. This result reveals significant research disparities among countries worldwide, with leading countries having a decisive advantage over others. There were 66 articles contributed by Chinese scholars, accounting for approximately 30% of all publications and producing an average citation rate of 15.06. The United States ranked second in terms of the number of publications, with 46 papers, which were cited 3227 times, for an average citation rate of 70.15. This finding indicates the central role of the United States in this field. In addition to China and the United States, the top five countries include Japan, South Korea, and Germany, indicating progress in these countries, likely as a result of significant government support for medical research, as most countries are developed nations. China
is the only developing country with the highest publication output, which can be attributed to the rapid growth in financial investment by the Chinese government in medical research, especially in cancer-related studies; this investment even surpasses that of most other countries except the United States. Additionally, with the world’s largest population, China provides ample patient resources for clinical research, which may contribute to the significant progress in medical research in China\[26,27\]. Importantly, despite China’s leading role in TJ proteins and CRC research, its partnerships with other nations/regions in this area are restricted; hence, China should intensify its collaborative efforts with other countries/regions. Figure 3A shows the collaboration among different countries; the United States is positioned at the center of the collaboration network, collaborating with multiple countries, including extensive collaboration with China. We also found that collaboration has become increasingly closer in recent years.

In terms of authorship analysis, Dhawan P from the United States had the highest number of publications, making him the most prolific scholar in this field. His research focused primarily on elucidating the mechanisms underlying the involvement of the TJ protein family member Cldn-1 in the development and progression of CRC. Among all the journals publishing related articles, Anticancer Research had the highest number of publications, followed by the International Journal of Molecular Sciences; the former is a journal focusing on oncology research, and the latter is a journal focused on molecular biology. Among the cited journals, Cancer Research ranked first in terms of the citation frequency, with a maximum impact factor of 11.2, followed by Oncogene and Gastroenterology, indicating the high academic influence of these journals in this research field. Notably, in the analysis of the articles cited in this study, the article titled “Claudin-1 regulates cellular transformation and metastatic behavior in colon cancer” published in 2005 had the highest number of citations[28]. This study demonstrated increased expression of claudin-1 in human primary CRC, metastases, and corres-
ponding cell lines, with claudin-1 expression detected in the cell nucleus. Claudin-1 induces phenotypic changes in CRC cell lines, leading to alterations in the structure and function of epithelial-mesenchymal transition markers. Furthermore, additional data suggest that the regulation of E-cadherin expression and β-catenin/Tcf signaling may be potential mechanisms underlying claudin-1-dependent changes.

In terms of keyword frequency, “colorectal cancer” and “expression” were the most prominent keywords, indicating that the majority of studies focused on the correlation between TJ protein expression and CRC. Additionally, “inflammatory bowel disease” is currently a hot topic. Keyword cluster analysis, keyword temporal distribution, and keyword burst analysis revealed that early-stage researchers are still in a relatively macroscopic and superficial stage of exploration regarding the association between CRC and TJ proteins. Researchers have attempted to determine the relationships between TJ protein expression and human colorectal adenomas and cancer. In the midterm, research directions gradually extended to the pathogenesis level, and to some extent, certain interactions between CRC and TJ proteins have been identified, with research primarily focusing on the TJ protein family members Cldn-1 and Cldn-7. In recent years, numerous studies have elucidated the relevance of TJ proteins to inflammatory bowel disease in the occurrence of CRC, further exploring the role of the intestinal microbiota in the association between TJ proteins and CRC occurrence.

This study has certain limitations. First, we included only articles published in English, excluding non-English publications from the bibliometric analysis, which may have interfered with the results. Second, the publications were retrieved only from the Web of Science database, which may have resulted in some publications not included in the database being overlooked. The Web of Science database, the most widely used bibliometric analysis database, was designed for this type of analysis[29]. Additionally, the Web of Science database rigorously evaluates publications, ensuring high-quality literature[29-31]. Third, recent high-quality publications have only been published for a short time, which may result in
lower citation counts. Therefore, citation frequency may not accurately reflect the quality of publications.

CONCLUSION
This bibliometric analysis evaluated the scope and trends of TJ proteins in CRC, providing valuable research perspectives and future directions for studying the connection between the two. The number of publications in the TJs and CRC field has grown steadily over the past two decades. It is recommended to focus on emerging hotspots such as the correlations among intestinal microbiota, inflammatory bowel disease, TJ protein expression, and CRC.

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FOOTNOTES

Author contributions: Li HM contributed to the conception and design of the study, and drafted and revised the manuscript; Liu Y and Hao MD are responsible for literature searching and data collection; Liang XQ and Yuan DJ are responsible for statistical analysis and charting; Huang WB and Li WJ checked the manuscript for grammar and spelling; Ding L coordinated the design and facilities for this study, provided multiple support in terms of personnel, materials and methods for the conduct of this study. All authors all approved the final manuscript.

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