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Research article

Knowledge mapping and current trends of m6A methylation in the field of cancer

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ABSTRACT

Background: Cancer is a serious threat to people's lives and health, killing millions of people every year. Here, we performed a bibliometric analysis of tumor N6-methyladenosine methylation data between 2001 and 2022 to understand research trends and potential future directions.
Methods: A total of 890 papers published in the Web of Science core collection database between January 1, 2001 and December 31, 2022 were analyzed. Bibliometric analysis was performed using VOSviewer software to explore citations, co-authorship, co-citations, and co-occurrence.
Results: Although few papers were published before 2018, there was a rapid increase in publications after 2018. The People's Republic of China published 810 papers with 16,957 citations, both ranking first in the word. Sun Yat Sen University had the highest number of citations and published articles (67 published papers and 2702 citations), indicative of its active collaborative research status. Wang Xiao was the most co-cited author with 546 co-citations. Huang Yufei and Meng Jia ranked first with a link strength of 22, making them the most active collaborative authors. Frontiers in Oncology and Nature were the most active and co-cited journals, with 57 papers and 1953 co-citations, respectively. Studies of tumor N6-methyladenosine methylation can be divided into three categories: "tumor metabolism", "tumor bioinformatics and immunity", and "tumor progression".
Conclusions: This study systematically summarized the research on tumor N6-methyladenosine methylation during the past 20 years and suggested potential ways to explore its biomarkers and immunotherapy in the future.

1. Introduction

Cancer is caused by the loss of normal regulation and excessive proliferation of cells. Cancer cells can invade surrounding tissues and metastasize to other organs through the circulatory system and/or lymphatic system. According to cancer statistics, 1,958,310 new cases and 609,820 deaths are estimated in the USA in 2023, and the incidence is higher in men than women [1]. Cancer is one of the leading causes of death in developed countries [2]. Although scientific advances have resulted in a decrease in cancer mortality in

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recent decades [1], further investigation remains essential in many fields.

RNA methylation is a stable and heritable modification that results in phenotype or gene expression changes without altering the nucleotide sequence [3]. RNA methylation is classified according to the modified position into N1-methyladenosine, 5-methylcytosine, N7-methylguanosine, and N6-methyladenosine (m6A) [4–6]. The m6A modification is the most common form of RNA methylation and plays important roles in regulating gene expression, splicing, RNA editing, RNA stability, mRNA lifespan control, and tumor development [7]. The m6A modification is closely related to the occurrence and development of tumors and has become a hot topic in cancer research [8–11].

Bibliometrics is an interdisciplinary science that consists of the quantitative analysis of all knowledge carriers using mathematical and statistical methods. It is a comprehensive knowledge system that integrates mathematics, statistics, and literature [12]. In 1969, Pritchard proposed the replacement of literature statistics with bibliometrics and extended the research scope from periodicals to all books [13]. Bibliometrics is widely used in scientific evaluation and management [14–16].

In this manuscript, we searched the literature on m6A methylation in the field of cancer from 2001 to 2022 to understand the current status of research in the field and to identify potential future directions.

2. Materials and methods

2.1. Data source and search strategy

Literature related to tumor m6A methylation was selected from the Web of Science (WOS) core collection database between January 1st, 2001 and December 31st, 2022. The search parameters were as follows: TS = ('m6A' OR 'N6-methyladenosine') AND ('methylation') AND ('cancer' OR 'carcinoma'). The language was limited to English, and the types of documents were limited to articles. The detailed data retrieval and inclusion processes are shown in Fig. 1.

2.2. Data collection and analysis

The file information was obtained from the WOS core collection database. All cited articles, including titles, authors, abstracts, keywords, journals, references, and citations, were downloaded. VOSviewer 1.6.18 was used to analyze the collaborative relationships among authors, organizations, and countries/regions through citation, co-authorship, and co-citation. High-frequency co-cited keywords and references were also clustered. The maps were presented in three modes: network, overlay, and density visualization. In the network visualization, different colors were used to indicate different clusters. The size of nodes was positively correlated with the total link strength or frequency of occurrence, and the line between nodes indicated the connection strength.

Microsoft excel was used to analyze and plot the number of annual publications related to tumor m6A methylation, as well as the top 10 most active authors, co-cited authors, institutions, and countries/regions, including the number of publications and citations. In addition, major journal information was analyzed and plotted, including impact factor (IF), journal citation reports (JCR) partition, number of published papers, countries, and total citations.

3. Results

3.1. Bibliometric analysis of publication output

In this study, 890 publications related to tumor m6A methylation between 2001 and 2022 were obtained from the WOS core collection database. As shown in Fig. 2, only one paper was published in 2001, and no related publications were retrieved in the following 12 years. After 2014, this field received increasing attention, and the highest number of publications was 347 in 2022. Fitting the curve of publication years revealed a significant relationship between number and year of publications. According to the curve, it is

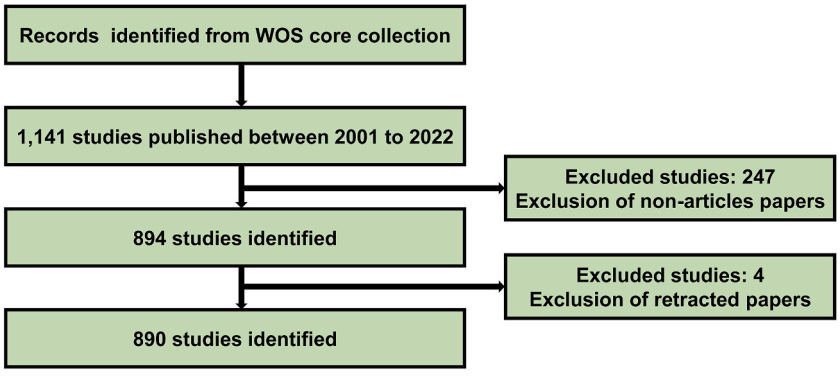

Fig. 1. Flow chart of the literature screening related to global research in the field of tumor m6A methylation.

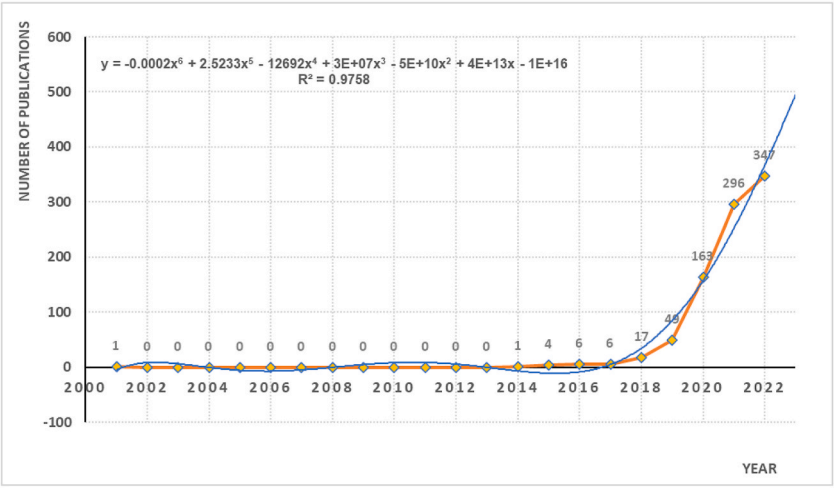

Fig. 2. Annual number of publications in the field of tumor m6A methylation between 2012 and 2021.

predicted that 500 papers related to tumor m6A methylation will be published in 2023. An increase in the number of experts entering into this field will result in an increasing number of publications in the future.

3.2. Bibliometric analysis of the publications and citations

As shown in Fig. 3A and Table 1, the most active authors were He Chuan and Zhang Lin. These authors both published 11 papers on tumor m6A methylation that were cited 1114 times and 324 times, respectively. Wang Wei followed with 10 papers. As shown in Fig. 3B and Table 2, 67 papers and 2702 citations were derived from Sun Yat Sen University, which ranked first among all organizations in publications and citations.

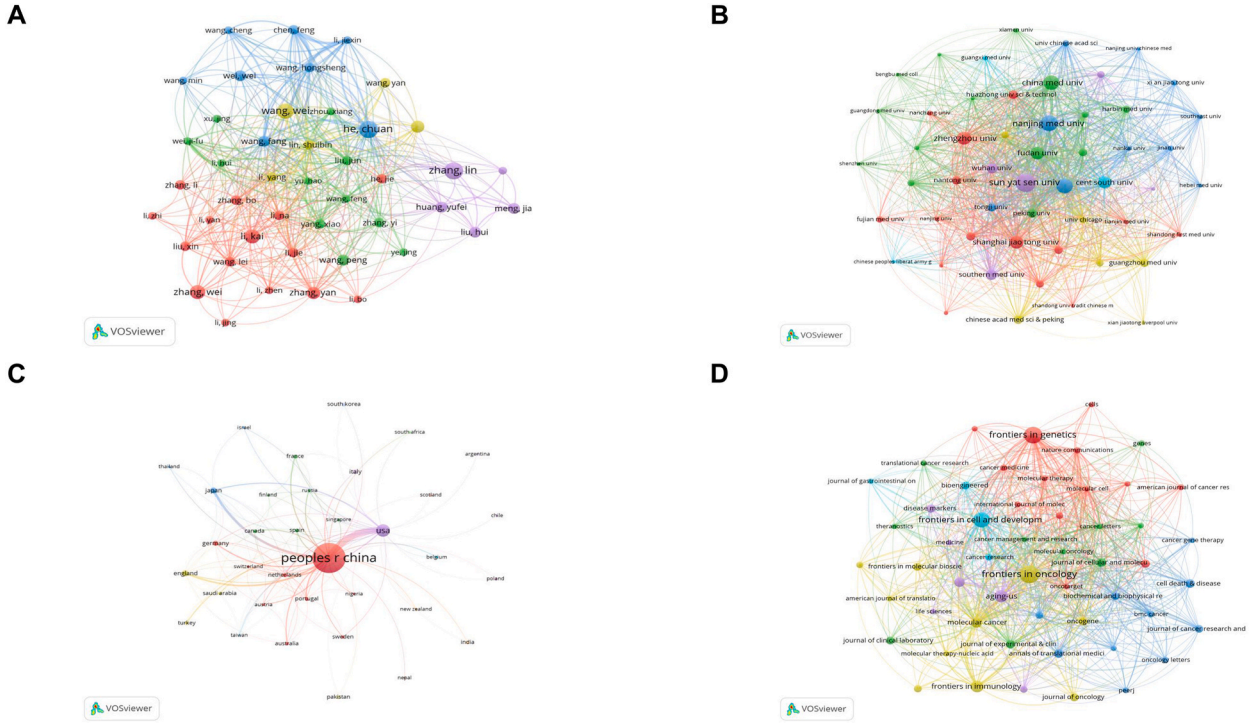

Fig. 3. Bibliometric analysis of publications in the field of tumor m6A methylation. **(A)** Bibliometric analysis of authors in the field of tumor m6A methylation. **(B)** Bibliometric analysis of institutions in the field of tumor m6A methylation. **(C)** Bibliometric analysis of countries/regions in the field of tumor m6A methylation. **(D)** Bibliometric analysis of journals in the field of tumor m6A methylation.

Table 1
Top 10 most active authors related to tumor m6A methylation.

Rank	Author	Number of publications	Count of citations
1	He Chuan	11	1114
2	Zhang Lin	11	324
3	Wang Wei	10	106
4	Li Kai	9	199
5	Zhang Wei	9	52
6	Zhang Yan	16	151
7	Zhang Qian	8	290
8	Wang Fang	8	685
9	Huang Yufei	7	392
10	Meng Jia	7	206

As shown in Fig. 3C and Table 3, People's Republic of China had the highest number of papers and citations, with a more than nine-fold higher number of publications than the USA (2nd place). Over the past two decades, People's Republic of China published 810 papers on tumor m6A methylation and has 16,957 citations.

As shown in Fig. 3D and Table 4, Frontiers in Oncology had 57 publications and 879 citations with an IF/JCR partition of 4.7/Q2, and it is thus the most active journal. Frontiers in Genetics and Frontiers in Cell and Developmental Biology ranked second and third, with 47 and 40 publications, respectively. Molecular Cancer had 17 publications in the field of tumor m6A methylation; however, the number of citations was 2,593, which is higher than that of other journals. This indicates that Molecular Cancer is an authoritative journal.

3.3. Bibliometric analysis of the co-authorship

3.3.1. Co-authorship analysis of countries/regions

As shown in Fig. 4A, People's Republic of China had the highest number of publications and cooperated most extensively with other countries. In the past two decades, 810 tumor m6A methylation papers were published, and the total link strength was 89. People's Republic of China has links with 18 countries, of which the USA is the largest partner with a link strength of 56. A study by researchers from People's Republic of China and the USA reported that reduction of m6A methylation may be related to activation of the AKT pathway, which promotes the proliferation and tumorigenicity of human endometrial cancer cells. The study also shows that m6A methylation is a regulatory factor in the AKT signaling pathway and associated with high expression of PHLPP2 and low expression of mTORC2 [17]. This finding has been cited 416 times since it was published in Nature Cell Biology in 2018 and it is one of the most popular articles. The total link strength for 91 publications in the USA was 86, which was comparable to that of People's Republic of China. This result may be due to the low level of cooperation with other countries despite the high number of articles published by People's Republic of China. Most of the articles published by People's Republic of China were completed by domestic researchers, whereas the USA produced many high-quality articles in cooperation with other countries. Therefore, international academic exchanges and cooperation can promote knowledge sharing as well as the renewal and development of academic fields.

The overlay visualization map (Fig. 4B) indicates that few countries published in the field of tumor m6A methylation after 2022; these countries include Nigeria, Saudi Arabia, and Poland. The analysis also revealed a downward trend in inter-state cooperation in recent years.

3.3.2. Co-authorship analysis of organizations

A total of 64 organizations with more than six publications were included in the co-authorship analysis (Fig. 5A). Sun Yat Sen University, which had partnerships with 33 organizations, was the most active institution, publishing 59 relevant papers with 2702 citations and a total link strength of 67. Nanjing Medical University and Shanghai Jiao Tong University followed with a total link strength of 40 and 38, respectively. Among them, Guangzhou Medical University and Southern Medical University were the closest partners of Sun Yat Sen University with a link strength of 7. A study performed in Sun Yat Sen University and Guangzhou Medical

Table 2
Top 10 most active organizations related to tumor m6A methylation.

Rank	Organizations	Number of publications	Count of citations
1	Sun Yat Sen University	67	2702
2	Nanjing Medical University	53	1893
3	Zhejiang University	49	1812
4	China Medical University	46	572
5	Zhengzhou University	41	684
6	Fudan University	39	977
7	Shanghai Jiao Tong University	38	1727
8	Central South University	36	534
9	Southern Medical University	29	560
10	Wuhan University	27	1018

Table 3
Top 10 most active countries/regions related to tumor m6A methylation.

Rank	Country	Number of publications	Count of citations
1	People's Republic of China	810	16,957
2	The USA	91	5182
3	Japan	14	528
4	England	12	383
5	Germany	9	111
6	Italy	8	176
7	Pakistan	6	37
8	Netherlands	4	251
9	Portugal	4	59
10	Spain	4	205

Table 4
Top 10 most active journals related to tumor m6A methylation.

Rank	Journal	Number	Citation	Country	IF/JCR partition (2022)
1	Frontiers in Oncology	57	879	Switzerland	4.7/Q2
2	Frontiers in Genetics	47	258	Switzerland	3.7/Q1
3	Frontiers in Cell and Developmental Biology	40	262	Switzerland	5.5/Q1
4	Aging-US	26	422	The USA	5.2/Q2
5	Frontiers in Immunology	22	188	Switzerland	7.3/Q1
6	Molecular Cancer	17	2593	England	37.3/Q1
7	Cancer Cell International	16	155	The USA	5.8/Q2
8	Annals of Translational Medicine	13	354	People's Republic of China	3.616/Q3
9	Cell Death & Disease	13	130	England	9/Q1
10	Journal of Cellular and Molecular Medicine	12	228	Romania	5.3/Q2

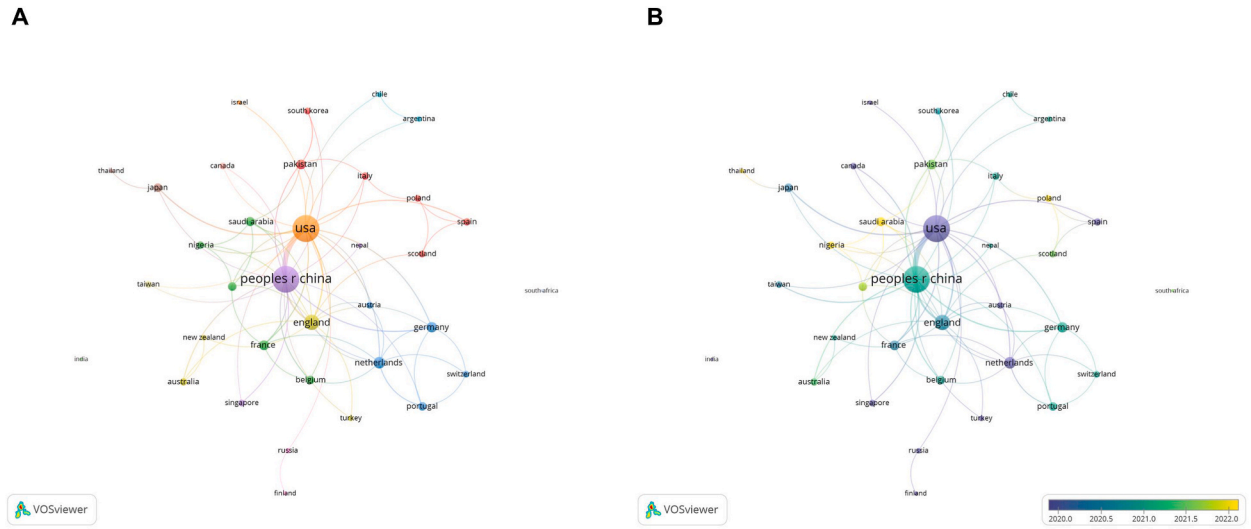

Fig. 4. Bibliometric analysis of co-authorship of countries/regions in the field of tumor m6A methylation. **(A)** Network visualization map of countries/regions involved in collaborations in the field of tumor m6A methylation. **(B)** Overlay visualization map of countries/regions involved in collaborations in the field of tumor m6A methylation.

University showed that the m6A demethylase FTO can promote the proliferation of breast cancer cells. This may be related to the FTO-mediated m6A demethylation of the 3′-untranslated region (3′-UTR) of the pro-apoptotic gene BNIP3 and the eventual degradation of BNIP3. This result identified FTO as a potential therapeutic target in breast cancer [18]. A study performed in Sun Yat Sen University and Southern Medical University reported that overexpression of FOXO3 restores m6A-dependent sorafenib sensitivity in hepatocellular carcinoma (HCC). This may be related to the m6A methylation of METTL3 to modify FOXO3 mRNA 3′-UTR and improve its stability. This result indicates that FOXO3 is an important target of m6A modification in sorafenib-resistant HCC [19]. These findings and the corresponding articles have been widely cited and demonstrate the importance of collaboration between organizations. China Medical University published 46 papers, ranking 4 among all organizations. However, the total link strength was only 9, which is mainly due to the lack of collaboration with other organizations.

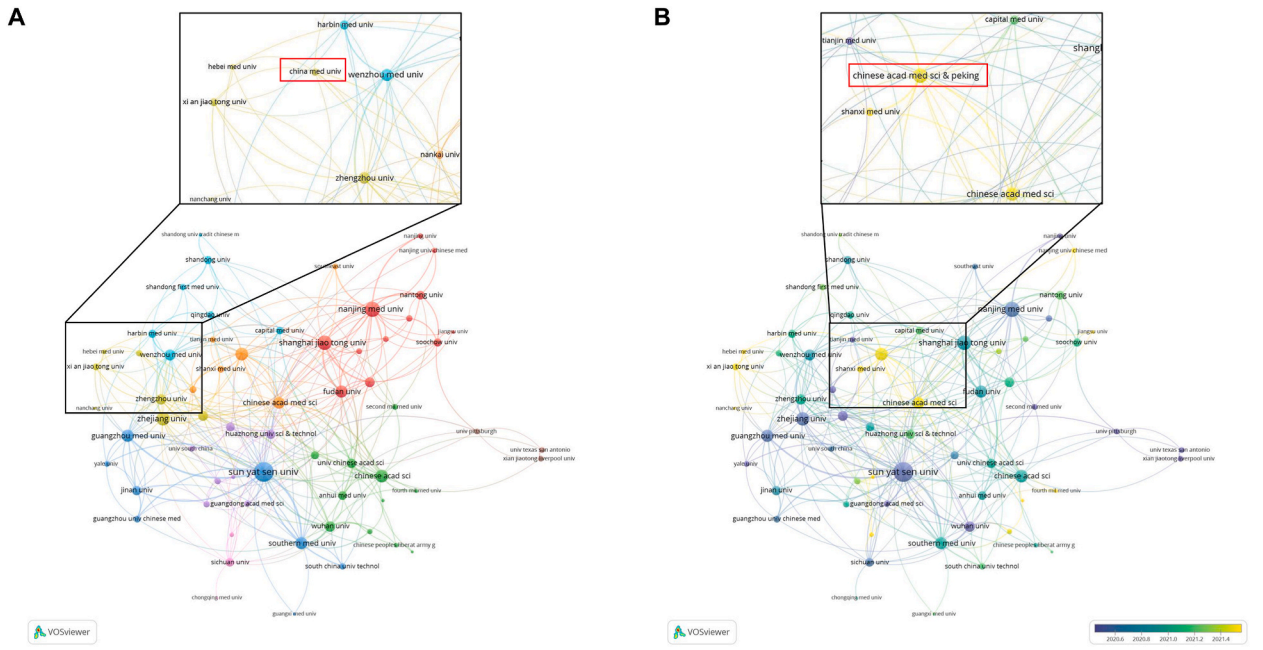

Fig. 5. Bibliometric analysis of the co-authorship of organizations in the field of tumor m6A methylation. **(A)** Network visualization map of collaborations among organizations in the field of tumor m6A methylation. **(B)** Overlay visualization map of collaborations among organizations in the field of tumor m6A methylation.

As shown in the overlay visualization map (Fig. 5B), Sun Yat Sen University, Zhejiang University, and Guangzhou Medical University were the main institutions conducting research in the field of tumor m6A methylation before June 2020. Subsequently, Chinese Academy of Medical Sciences & Peking, followed by Chinese Academy of Medical Sciences, Xi An Jiao Tong University and Shanxi Medical University became the most popular organizations after April 2021. Chinese Academy of Medical Sciences & Peking mainly studied the role of m6A methylation in the occurrence and development of tumors such as gastric cancer (GC) [20], endometrial cancer [21], and esophageal squamous cell carcinoma [22].

3.3.3. Co-authorship analysis of authors

A total of 91 authors of more than four papers were selected for co-authorship analysis. In the network visualization map (Fig. 6A), Huang Yufei and Meng Jia tied for the first place, with a total link strength of 22. These authors collaborated with other authors, mainly

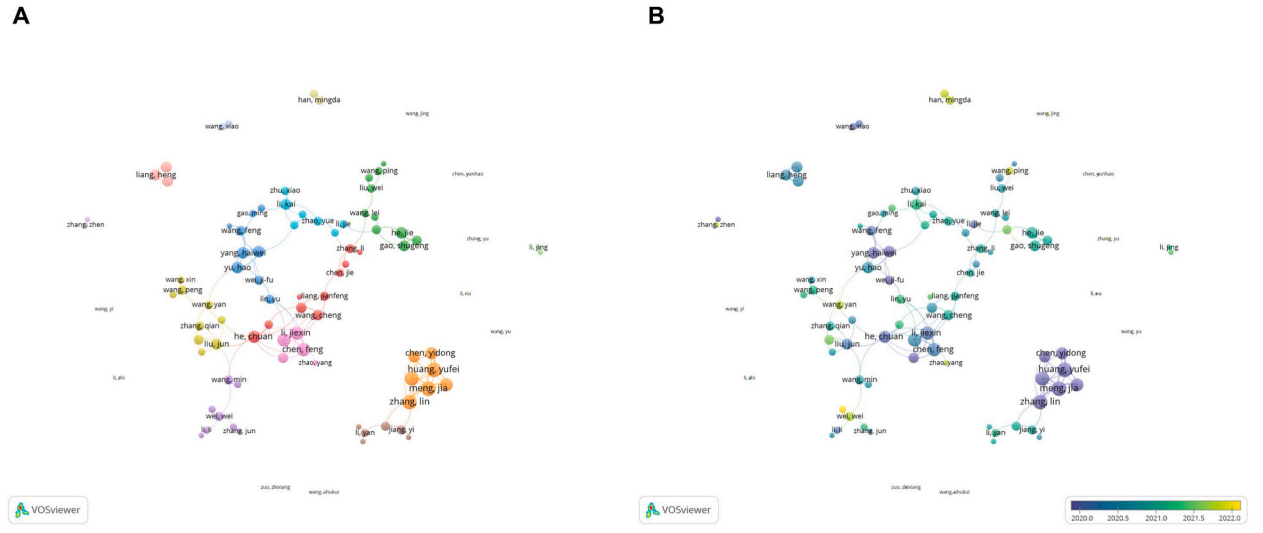

Fig. 6. Bibliometric analysis of the co-authorship of authors in the field of tumor m6A methylation. **(A)** Network visualization map of author collaborations in the field of tumor m6A methylation. **(B)** Overlay visualization map of author collaborations in the field of tumor m6A methylation.

in small groups with Zhang Lin, Chen Yidong and others. One of their studies reported that the carcinogenic Kaposi's sarcoma-associated herpesvirus (KSHV) can induce m6A and m6Am (m6A/m) hypomethylation at the 5′-UTR as well as m6A/m hypermethylation at the 3′-UTR of the cellular epitranscriptome in the latent phase. This phase can regulate carcinogenesis and epithelial-mesenchymal transformation pathways, which are critical for the development of KSHV-associated cancers [23]. Certain authors focused on individual research and did not form a team, such as Chen Yunhao, Li Na, and Wang Jing. However, their achievements in the field of tumor m6A methylation cannot be ignored. For example, Chen et al. [24] first reported that Wilms tumor 1-associated protein (WTAP)-mediated m6A methylation can lead to post-transcriptional suppression of the downstream effector ETS1, thereby inhibiting the tumorigenesis of HCC. These results showed that WTAP-mediated m6A methylation plays a crucial role in HCC development, identifying WTAP as a potential therapeutic target for HCC.

The overlay visualization map (Fig. 6B) shows that Zhang Yu became interested in the field of tumor m6A methylation after 2022. His group identified a novel therapeutic approach for the treatment of gefitinib-resistant non-small cell lung cancer through FTO-mediated N6-demethylation in combination with meclofenamic acid [25].

3.4. Bibliometric analysis of the co-citations

As shown in Fig. 7A, 108 co-cited authors with more than 50 co-citations were selected for bibliometric analysis. The top 10 co-cited tumor m6A methylation authors are listed in Table 5. Wang Xiao ranked first with 546 co-citations, followed by Meyer KD with 393 co-citations and Dominissini D with 509 co-citations.

In Fig. 7B–a total of 159 co-cited references were selected for the density visualization map. The top 10 co-cited references related to tumor m6A methylation are listed in Table 6, including the number of co-citations and IF/JCR. Wang et al. [26] published an article titled "N6-methyladenosine-dependent regulation of messenger RNA stability" in Nature in 2014, which was co-cited 251 times. The study showed that dynamic m6A modifications are recognized by selective binding proteins and thus affect mRNA translation status and lifespan. The manuscripts of Dominissini et al. [27] and Chen et al. [28] ranked second and third, respectively. Two papers published in Nature took first and second place, respectively.

As shown in Figs. 7C and 145 co-cited journals with more than 50 co-citations were selected for the density visualization map. The top 10 co-cited journals are shown in a graph in Fig. 7D. Nature was the most co-cited journal with 1953 co-citations, followed by Molecular Cancer with 1741 co-citations and Cell with 1497 co-citations. Molecular Cancer appeared in both the top 10 most active and co-cited journals, demonstrating the authority of the journal.

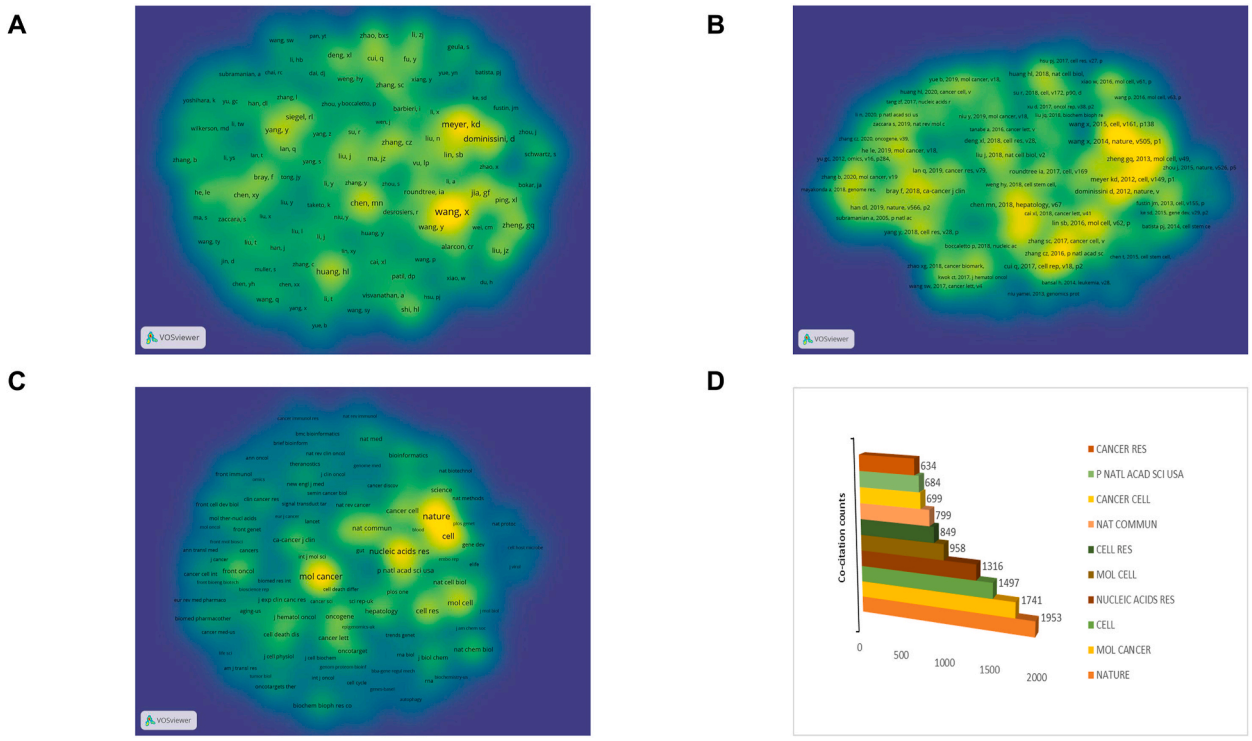

Fig. 7. Bibliometric analysis of co-citations in the field of tumor m6A methylation. **(A)** Density visualization map of co-cited authors in the field of tumor m6A methylation. **(B)** Density visualization map of co-cited references in the field of tumor m6A methylation. **(C)** Density visualization map of co-cited journals in the field of tumor m6A methylation. **(D)** Top 10 main co-cited journals related to tumor m6A methylation.

Table 5
Top 10 co-cited authors related to tumor m6A methylation.

Rank	Co-cited Author	Count of co-citation
1	Wang, X	546
2	Meyer, KD	393
3	Dominissini, D	281
4	Chen, MN	267
5	Huang, HL	230
6	Jia, GF	228
7	Yang, Y	210
8	Zhang, CZ	195
9	Lin, SB	195
10	Zheng, GQ	183

Table 6
Top 10 co-cited references related to tumor m6A methylation.

Rank	Co-cited reference	Count	IF/JCR partition (2022)
1	Wang X, 2014, Nature, v505, p117	251	64.8/Q1
2	Dominissini D, 2012, Nature, v485, p201	232	64.8/Q1
3	Chen MN, 2018, Hepatology, v67, p2254	222	13.5/Q1
4	Jia GF, 2011, Nat chem biol, v7, p885	202	14.8/Q1
5	Meyer KD, 2012, Cells, v149, p1635	183	6/Q2
6	Lin SB, 2016, Mol cells, v62, p335	180	3.8/Q2
7	Zheng GQ, 2013, Mol cells, v49, p18	179	3.8/Q2
8	Liu JZ, 2014, Nat chem biol, v10, p93	179	14.8/Q1
9	Wang X, 2015, Cells, v161, p1388	178	6/Q2
10	Cui Q, 2017, Cell rep, v18, p2622	169	8.8/Q1

3.5. 3.5 bibliometric analysis of co-occurrence keywords

VOSviewer was used to construct a keyword network map with an extraction frequency >20, resulting in the identification of 77 high-frequency keywords (Fig. 8A). High-frequency keywords were divided into three categories as follows: cluster 1: “tumor metabolism” (red), including methylation, translation, and metabolism; cluster 2: “tumor bioinformatics and immunity” (green), including prognosis, immunotherapy, biomarkers, and TCGA; and cluster 3: “tumor progression” (blue), including expression, proliferation, and metastasis. In addition, we identified several effective high-frequency keywords that had a large number of co-occurrences in >100 cases, potentially representing an important research area in the field of tumor m6A methylation. These keywords mainly included expression, prognosis, progression, and proliferation.

The overlay visual analysis of high-frequency keywords (Fig. 8B) indicated that the research direction in tumor m6A methylation may transition from tumor metabolism to tumor progression, and finally to prognosis and treatment. This indicates that therapeutic approaches are an area of interest for researchers at this stage. Biomarkers, immunotherapy, tumor microenvironment, and other keywords are currently research hotspots in tumor m6A methylation. This result indicates that many researchers aim to identify potential biomarkers, and cancer immunotherapy has become a new research direction.

4. Research hotspots and frontiers

Based on the results of the bibliometric analysis, we discuss several hotspots and frontiers of tumor m6A methylation.

4.1. The interaction between m6A methylation and long non-coding RNA (lncRNA) expression in tumor progression

The interaction between m6A methylation and certain lncRNAs can affect the occurrence and development of tumors. Fig. 8 illustrates this interaction and shows that the association is particularly strong in lung, liver, and GC.

In lung cancer, Yu et al. [29] demonstrated that ALKBH5 upregulates the lncRNA RMRP through m6A demethylation, thereby promoting the occurrence of lung adenocarcarcinoma (LUAD). Modulation of ALKBH5 to inhibit RMRP could be a therapeutic strategy for LUAD. METTL3-mediated modification of m6A methylation can increase the stability of the lncRNA LCAT3 and lead to its upregulation. Overexpression of LCAT3 activates MYC transcription and promotes growth, invasion, and metastasis in LUAD [30]. The lncRNAs AC098934, HOTAIR, and SNHG17 are regulated in an m6A-dependent manner, thus affecting the malignant behavior of lung cancer [31–33].

Wu et al. [34] showed that METTL3 regulates the m6A modification of lncRNA MEG3 and its expression, and modulates BTG2 expression through miR-544b, inhibiting growth and invasion in HCC. A later study showed that METTL3-dependent m6A methylation leads to overexpression of the lncRNA NIFK-AS1 in HCC tissues and cells, which promotes HCC cell growth and invasion through the miR-637/AKT1 signaling pathway [35]. Zhang et al. [36] reported that the lncRNA LINC02551 is downregulated by ALKBH5 in an

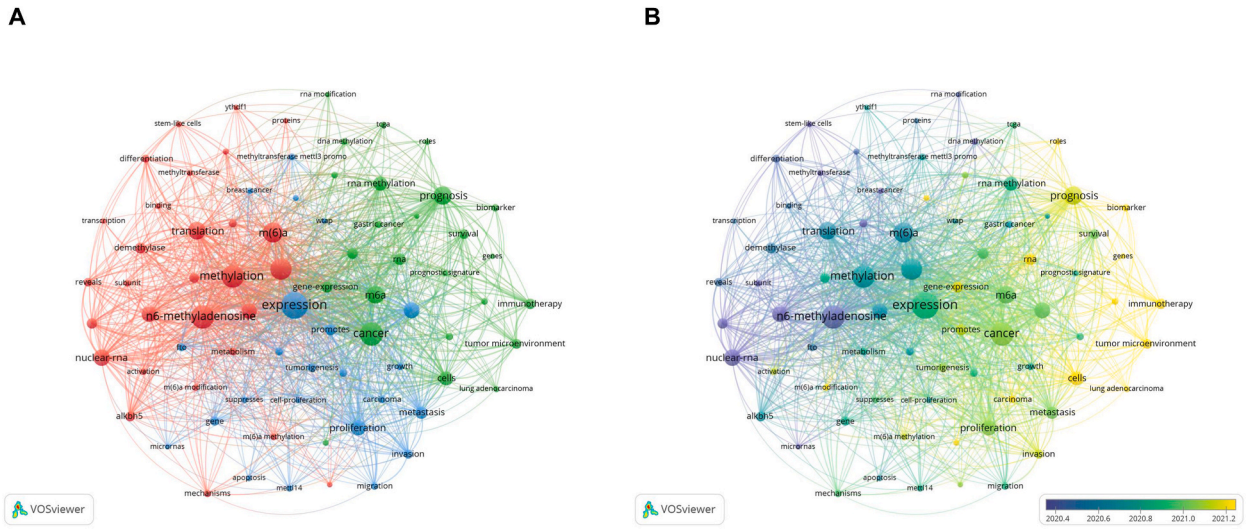

Fig. 8. Bibliometric analysis of the co-occurrence of all keywords in the field of tumor m6A methylation. **(A)** Network visualization map of high frequency keywords in the field of tumor m6A methylation. **(B)** Overlay visualization map of high frequency keywords in the field of tumor m6A methylation.

m6A-dependent manner in HCC, leading to the ubiquitination and degradation of DDX24 and ultimately promoting HCC proliferation and metastasis. Studies show that the expression of the lncRNAs LINC00958, DUXAP8, MIR155HG, and ARHGAP5-AS1 is modulated in an m6A-dependent manner, which affects their downstream target genes and thus the biological behavior of HCC [37–40].

Microarray gene expression profiling and bioinformatics analysis combined with other technologies were used to identify m6A-related lncRNAs that may play a role in the development and prognosis of GC [41–44]. Yang et al. [45] showed that the hypoxic-inducible lncRNA CBSLR regulates ferroptosis in GC by modulating the m6A-YTHDF2-dependent regulation of CBSLR. Hu et al. [46] reported that METTL14 regulates the modification of LINC01320 by m6A methylation. Overexpression of LINC01320 promotes invasion in GC cells by modulating the miR-495-5p/RAB19 signaling pathway, providing a novel target for the treatment of GC. Similar results indicate that the lncRNA LINC02253 positively modulates cell proliferation and metastasis by increasing the stability of KRT18 mRNA mediated by METTL3 [47]. ALKBH5 decreases the stability of the lncRNA TP53TG1 in an m6A-dependent manner, promoting PI3K/AKT pathway activity and leading to GC cell proliferation and metastasis [48].

4.2. m6A methylation and tumor metabolism

The m6A methylation modification can affect tumorigenesis and development by interfering with tumor metabolism. Liu et al. [49] demonstrated that ALKBH5 plays an important role in mediating the proliferation and energy metabolism of glioma cells through m6A methylation.

m6A methylation is involved in the regulation of tumor RNA metabolism. Shah et al. [50] showed that DDX3 interacts with ALKBH5, an m6A demethylase, thereby affecting tumor RNA metabolism. Suppression of ALKBH5 inhibits myeloma cell angiogenesis, proliferation, and RNA metabolism, suggesting its potential as a biomarker in myeloma [51]. Similar results indicated that METTL3 increases CDC25B mRNA metabolism and m6A methylation modification, promoting the malignant progression of HNSCC [52].

In terms of glucose metabolism, Tan et al. [53] revealed that ALKBH5 is associated with glucose metabolism in neuroblastoma, and this prognostic model has high application value for predicting and evaluating the prognosis of neuroblastoma patients. Another research group demonstrated that METTL3 is involved in the modulation of glycolytic activity, suggesting that inhibition of glucose metabolism by METTL3 suppression is a potential therapeutic strategy for HCC [54]. Du et al. [55] indicated that METTL14 regulates glycolysis to inhibit HCC, providing new insight into the role of HCC metabolic activity. Xu et al. [56] showed that NDUFA4 is upregulated through m6A methylation and promotes GC development by increasing glucose metabolism and mitochondrial fission.

m6A methylation is also involved in the cellular and molecular metabolism of tumors. Peng et al. [57] reported that METTL3 is involved in cellular metabolism in GC cells through an m6A-dependent mechanism, suggesting its value as a prognostic marker in GC. An in-depth study revealed that the m6A related protein YTHDF1 plays a vital role in the regulation of HCC cell cycle metabolism [58]. Abnormal iron metabolism is another hot topic in cancer research. The results of Huang et al. [59] elucidated a mechanism by which ALKBH5 protects pancreatic ductal adenocarcinoma by regulating iron metabolism regulators and highlighted the key role of m6A methylation. Another study found that YTHDF1 promotes hypopharyngeal squamous cell carcinoma tumorigenesis dependent on abnormal iron metabolism by increasing the expression of TFRC through an m6A-dependent mechanism [60].

4.3. m6A methylation and tumor immunity

The immune function of the body is closely related to the occurrence and development of tumors [61]. The immune response to tumors and the mechanisms underlying antitumor immunity are research hotspots [62,63]. Tumor immunotherapy is a treatment that aims to control and eliminate tumors by restarting and maintaining the tumor-immune cycle and restoring the normal antitumor immune response of the body [64,65]. Recent studies show that m6A methylation plays an important role in regulating the tumor immune microenvironment, immune cell infiltration, and immunotherapy [66,67].

As shown in Fig. 8A, m6A methylation is closely related to immunity in a variety of tumors, especially bladder cancer (BCa) and prostate cancer (PCa). Wang et al. [68] showed that METTL3 with copy number variations is associated with immune cell infiltration and could be used as a prognostic marker for BCa. The JNK signaling pathway promotes tumor immune escape in vitro and in vivo through a METTL3-dependent mechanism, leading to the progression of BCa [69]. Zhao et al. [70] used bioinformatics methods to identify two genes related to immune infiltration, PGM1 and ENO1, which affect the malignant progression of BCa. Researchers identified m6A and immune-related lncRNAs from cancer databases and established risk models for predicting the prognosis, immune efficacy, and chemotherapy response in BCa [71–73]. In PCa, Ye et al. [74] used a dataset to analyze the relationship between methylation-related genes and the tumor microenvironment, and explored how this affects prognosis, tumor mutation burden, and immunotherapy reactivity in PCa. Another research group developed a risk prediction model using 24 m6A regulators, providing an option for predicting prognosis and designing personalized immunotherapy for PCa patients [75].

4.4. m6A methylation and tumor bioinformatics

Bioinformatics is an interdisciplinary science that includes the acquisition, processing, storage, distribution, analysis, interpretation, and other aspects of biological information [76]. It combines the tools of mathematics, computer science, and biology to elucidate and understand the biological implications of large amounts of biological data. Increasing evidence supports the important role of bioinformatics in tumor detection, treatment, and prognosis.

Knowledge graph analysis indicates that many researchers use bioinformatics to construct m6A- and tumor-related models to predict the prognosis of patients. Qiu et al. [77] generated a prognostic model consisting of seven m6A-related lncRNAs associated with the expression of immune checkpoints and immune cell infiltration. This seven m6A-related lncRNA model will contribute to the management of clear cell renal cell carcinoma patients and guide individualized immunotherapy. Jia et al. [78] constructed a prognostic risk model using three m6A-related genes (MT1E, FAM71F1, and MYEOV), which could be of value for the prognosis of lung cancer and tumor-related immune cell infiltration. A prediction model consisting of three m6A-related regulators and four ferroptosis regulators was constructed and shown to predict the prognosis of pancreatic cancer more effectively than previous single-genome or epigenetic analyses [79]. Several prediction models have shown efficacy for the clinical diagnosis and treatment of cancers such as BCa [80], colorectal cancer [81], HCC [82], and glioma [83].

5. Strengths and limitations

This study is the first to perform a comprehensive and systematic bibliometric analysis of the literature on tumor m6A methylation. The findings could serve as an effective guide for clinicians working in the field and help researchers search for collaborations. This study had some limitations. First, the literature search was limited to the WOS core collection database, and no other databases were searched. Second, the VOSviewer analysis was based only on the main information provided by the papers and not the full text. Third, some newly published high-quality papers may not receive enough attention, resulting in citation rates that are often lower than those of classic papers.

6. Conclusion

This study consisted of a comprehensive analysis of the status of tumor m6A methylation research during the period between 2001 and 2022. Since 2018, the field of tumor m6A methylation has gained increasing attention. People's Republic of China has made an important contribution to this field. Countries should actively create opportunities for communication and cooperation to promote the balance of regional academic development. The exploration of biomarkers and immunotherapy may become the main research direction in the future.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Data availability statement

Not applicable.

CRediT authorship contribution statement

Chunming Zhu: Formal analysis, Investigation, Methodology, Software, Writing – original draft. **Jun Yang:** Data curation, Funding acquisition, Software, Validation. **Chengpu Zhang:** Supervision, Visualization. **Yibing Wang:** Investigation, Methodology, Software, Visualization. **Jiahe Wang:** Conceptualization, Funding acquisition, Supervision, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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