# Original Article Global research hotspots and trends of the Notch signaling pathway in the field of cancer: a bibliometric study

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**Abstract:** Objectives: To analyze the development status, research hotspots, research frontiers and future development trends of the Notch signaling pathway in cancer through bibliometric analysis. Methods: Publications related to the Notch signaling pathway in cancer were obtained from the Web of Science Core Collection (WoSCC), and information was extracted from the articles using Microsoft Excel 2020, CiteSpace V and VOSviewer software for visual analysis. Results: The country and institution with the most publications are the USA and Harvard University, respectively. PLoS One is the most published journal, and Cancer Research is the most cocited journal. The author with the most published articles was L Miele, and the most cocited author was ZW Wang. The top 3 keywords were activation, differentiation and growth. Metastasis, epithelial-mesenchymal transition (EMT), invasion, target and resistance are the current research hotspots and frontiers in this field. Conclusions: Research related to the Notch signaling pathway in cancer is currently booming, and the USA has made the greatest contribution to this field. At present, the research hotspots and research frontiers in this field mainly focus on the regulatory role of the Notch signaling pathway in tumor invasion and metastasis, the regulation of the Notch signaling pathway in tumor invasion of the Notch signaling pathway in tumor invasion and metastasis, the regulation of the Notch signaling pathway in tumor invasion and metastasis, the regulation of the Notch signaling pathway in tumor invasion and metastasis, the regulation of the Notch signaling pathway in tumor progression through EMT, and the participation of the Notch signaling pathway in the regulation of chemotherapy or immunotherapy resistance to tumors.

Keywords: Bibliometric, Notch, EMT, resistance, metastasis

#### Introduction

The Notch signaling pathway is a highly conserved signaling pathway in vertebrates and invertebrates [1]. The Notch gene was first identified in Drosophila and named because its mutations can cause notches in Drosophila wings [2]. Notch is one of the most important pathways that determines cell fate. The Notch signaling pathway is mainly composed of four parts: Notch receptor, Notch ligand, CSLDNA binding protein and downstream target genes [3]. Changes in any of the above four factors will affect the transmission of the Notch signaling. The pathogenesis of tumors is very complex and remains to be elucidated. The Notch signaling pathway has been extensively involved in tumorigenesis and development [4]. It may play an oncogenic role, leading to the dysregulation

of cell proliferation, cycle, differentiation, and apoptosis, thus causing the malignant transformation of cells and ultimately causing tumorigenesis [5-8]. In general, in-depth studies of the Notch signaling pathway will help us to master its mechanism and provide insights for the treatment of cancer.

Bibliometrics is an interdisciplinary field that can enable quantitative analyses of the literature using mathematical and statistical methods [9]. Bibliometrics was first proposed by American bibliographers in 1969, and after several decades of development, it gradually became a mature discipline [10]. With advances in scientific research, an increasing number of papers have been published, under such a large amount of information, researchers often find it difficult to identify truly useful information



and may be misled. Bibliometric analysis is essential for preventing the above situation because it can not only help understand the research output of specific fields but also help scholars grasp the current research hotspots and research frontiers in the field as quickly as possible, thus guiding future research directions. Currently, bibliometrics has been applied in various fields, such as the Wnt signaling pathway, cataracts, exosomes, and macrophage polarization [11-14].

Although many studies have focused on the Notch signaling pathway in cancer, bibliometric studies have not been performed on this pathway. This study aims to visualize the research outputs, research hotspots and research frontiers in this field through bibliometric analysis, so as to help understand future directions in the development of basic and clinical research in this field.

#### Materials and methods

#### Data collection

We retrieved data from the literature from the Web of Science Core Collection (WoSCC) and downloaded all the required data on December 31, 2021. Our retrieval strategy was as follows: TS = ("Notch") AND TS = ("Tumor\*" OR "Neoplasm\*" OR "Neoplasia\*" OR "Cancer\*"). The date was set from 1 January 2001 to 31 December 2021, the language was limited to English, and the literature type was limited to articles. We exported the retrieved literature as "full record and cited references" and saved it as text files for subsequent analyses. The process of the literature search is shown in **Figure 1**.

### Data analysis

The software used in this study included Microsoft Excel 2020, CiteSpace V, and VOSviewer. We used Microsoft Excel 2020 to analyze the number of articles per year and their growth trends. CiteSpace V is a Java-based software developed by Professor Chen Chaomei of Drexel University for bibliometric

analysis and data visualization [15]. This study mainly used CiteSpace V to analyze the keyword and reference bursts. VOSviewer software was developed by the Center for Science and Technology Research at Leiden University, and it can be used for visualization analyses of data and construction of a wide variety of network relationships [16]. The distribution of publications among countries, institutions, journals, authors, and their partnerships was analyzed and visualized using VOSviewer. Keyword clustering in this study was also performed using VOSviewer to generate visual network maps. In addition, discipline and journal analyses were conducted using the dual-map overlay of CiteSpace V.

The downloaded data were imported into CiteSpace V and VOSviewer for further analysis. The time span was from 2001 to 2021, and the time slice was 1 year. For the cooperative network analysis, we selected four node types: country, institution, author and journal. Keywords were selected for the cooccurrence and burst analyses. References were selected for the cocitation and burst analyses. We set the links parameters to "Strength: Cosine" and "Scope: Within Slices". The remaining parameters were set to the default values.

## Results

## Trend of publication outputs

The number of papers published per year can reflect trends in a given area of research. We



Figure 2. Annual number and growth trends of publications from 2001 to 2021.

used Microsoft Excel 2020 to analyze the number of articles per year and their growth trends. The results showed that 6494 papers about the Notch signaling pathway in cancer were published from 2001 to 2021. Before 2005, fewer than 100 papers were published each year. Since 2007, an explosive and sustained increase in the number of papers has been observed in this field, and it peaked in 2021 (**Figure 2**). These results indicate that the Notch signaling pathway in cancer has attracted increasing attention over the past 20 years and will continue to be the focus of attention for a long time in the future.

### Distribution of countries/regions and institutions

A total of 91 different countries/regions and 5310 different institutions have published papers about the Notch signaling pathway in cancer. The top 10 countries/regions and institutions are listed in Table 1. The largest number of publications were from the USA (2596, 39.97%), followed by China (1961, 30.19%). The number of papers from China and the USA accounts for more than 70% of the total number, indicating that these two countries have made great contributions to this field. Centrality is a reflection of influence. Although China has published many papers, its centrality was much lower than that of the USA (0.06 vs. 0.90), indicating that the USA has far greater influence in this field than China. Although research related to the Notch signaling pathway in cancer started late in China, the rate of development is amazing. Since 2011, China's research output in this field has been increasing at an alarming rate, and it surpassed the USA in 2017 to become the country with the most annual publications in this field (Figure 3A). Harvard University had the largest number of publications (166, 2.55%) and the highest centrality (0.31). Figure 3B shows the cooperation between countries/regions. Each node represents a country, and larger nodes indicate a larger number of publications. Lines between nodes represent cooperation between countries, and thicker lines rep-

resent closer cooperation. As seen from the figure, the USA, China, and Japan have formed stable cooperative relations. In addition, Germany, Italy, the Netherlands and Switzerland have also formed good cooperation networks. **Figure 3C** shows the cooperation between various institutions. The red cluster is composed of local Chinese institutions, and full cooperation is observed between them. The purple cluster forms a cooperative network centered on Harvard University, and the blue cluster forms a cooperative network centered on the University of Pennsylvania.

## Authors and cocited authors

The top 10 authors in terms of the number of publications are shown in **Table 2**. L Miele is the author with the most published papers (47, 0.72%). The network diagram shows that there is a lack of deep cooperation between authors (**Figure 4A**). Cocited authors refer to two or more authors who are simultaneously cited by another paper or more papers, and these two or more authors form a cocited relationship. Among the top 10 cocited authors, 4 authors had a centrality above 0.1, indicating that these authors (**Table 2**). The network of cocited authors shows that a good cocited relationship has been formed among authors (**Figure 4B**).

#### Journals and cocited journals

A total of 1163 journals published papers related to the Notch signaling pathway in cancer, and the top 10 journals in the number of pub-

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Rank	Country/region	Count (%)	Centrality	Year	Institution	Count (%)	Centrality	Year
1	USA	2596 (39.97)	0.90	2001	Harvard Univ	166 (2.55)	0.31	2001
2	China	1961 (30.19)	0.06	2008	Univ Texas MD Anderson Canc Ctr	121 (1.86)	0.06	2008
3	Japan	413 (6.35)	0.08	2007	Shanghai Jiao Tong Univ	105 (1.61)	0.04	2012
4	Germany	388 (5.97)	0.11	2008	Johns Hopkins Univ	96 (1.47)	0.12	2001
5	England	319 (4.91)	0.07	2008	Sun Yat Sen Univ	95 (1.46)	0.06	2013
6	Italy	309 (4.75)	0.12	2007	Univ Michigan	93 (1.43)	0.03	2009
7	South Korea	236 (3.63)	0.04	2007	Fudan Univ	90 (1.38)	0.02	2013
8	Canada	218 (3.35)	0.04	2008	National Cancer Institute	83 (1.27)	0.04	2001
9	France	210 (3.23)	0.12	2008	Univ Penn	77 (1.18)	0.06	2003
10	Spain	178 (2.74)	0.05	2008	Harvard Med Sch	71 (1.09)	0.02	2003

Table 1. Top 10 countries/regions and institutions with the largest number of publications



Figure 3. (A) Number of publications per country per year; (B) Cooperation between countries/regions; and (C) cooperation between various institutions.

lished papers are shown in **Table 3**. PLoS One is the most highly published (233, 3.58%), followed by Cancer Research (203, 3.12%) and Oncotarget (174, 2.67%). An analysis of the top 10 journals with the most cocitations shows that Cancer Research has the most cocitations (**Table 3**). In addition, the centrality of 5 of the top 10 journals exceeded 0.1, indicating that

the 5 journals had a large influence. **Figure 5A** shows the network of cocited journals, and it is clear that cocitation relationships were formed between most journals. The referential relationship of academic journals represents the situation of knowledge exchange in the research field in question, where the citing papers form the frontier of knowledge, and the cited papers

Rank	Author	Count (%)	Centrality	Cocited author	Count	Centrality
1	L Miele	47 (0.72)	0.02	ZW Wang	912	0.09
2	JC Aster	32 (0.49)	0.01	AP Weng	830	0.16
3	H Han	29 (0.44)	0.01	S Artavanis-Tsakonas	806	0.52
4	FH Sarkar	28 (0.43)	0.00	M Katoh	706	0.01
5	ZW Wang	27 (0.41)	0.01	R Kopan	705	0.15
6	H Chen	27 (0.41)	0.00	F Radtke	610	0.12
7	CG Eberhart	27 (0.41)	0.01	M Reedijk	459	0.02
8	AL Harris	26 (0.40)	0.00	L Miele	424	0.04
9	X Chen	21 (0.32)	0.02	SJ Bray	420	0.08
10	W Wang	21 (0.32)	0.01	KG Leong	409	0.03

 Table 2. Top 10 authors and cocited authors



Figure 4. (A) Network map of active authors; and (B) network map of cocited authors.

Rank	Journal	Count (%)	IF	Cocited journal	Count	Centrality	IF
1	PLoS One	233 (3.58)	3.24	Cancer Research	12612	0.18	12.70
2	Cancer Research	203 (3.12)	12.70	Nature	12197	0.11	49.96
3	Oncotarget	174 (2.67)	4.14	Proceedings of the National Academy of Sciences of the USA	9956	0.17	12.20
4	Oncogene	129 (1.98)	9.86	Cell	8735	0.29	41.58
5	Scientific Reports	95 (1.46)	4.37	Journal of Biological Chemistry	7396	0.05	5.15
6	Journal of Biological Chemistry	92 (1.41)	5.15	Oncogene	6385	0.06	9.86
7	Oncology Reports	90 (1.38)	3.90	Development	6365	0.08	6.86
8	Clinical Cancer Research	82 (1.26)	12.53	Science	5908	0.05	47.72
9	Proceedings of the National Academy of Sciences of the USA	82 (1.26)	11.20	Blood	5394	0.04	22.11
10	Oncology Letters	80 (1.23)	2.96	Genes & Development	5110	0.13	11.36

Table 3. Top 10 journals and cocited journals

form the knowledge basis. **Figure 5B** shows a dual-map overlay of journals. The left side of the figure shows the citing journal, the right

side shows the cited journal, and the lines between them represent the cited relationships. As we can see from the figure, the yellow

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Figure 5. (A) Network of cocited journals; and (B) dual-map overlay of journals.

Rank	Cocited reference	Count	Centrality	Year
1	Artavanis-Tsakonas S, 1999, Science, V284, P770	803	0.11	1999
2	Kopan R, 2009, Cell, V137, P216	492	0.21	2009
3	Weng AP, 2004, Science, V306, P269	480	0.30	2004
4	Bray SJ, 2006, Nat Rev Mol Cell Bio, V7, P678	324	0.05	2006
5	Ellisen LW, 1991, Cell, V66, P649	311	0.17	1991
6	Van Es JH, 2005, Nature, V435, P959	297	0.04	2005
7	Noguera-Troise I, 2006, Nature, V444, P1032	296	0.08	2006
8	Reedijk M, 2005, Cancer Res, V65, P8530	292	0.03	2005
9	Radtke F, 2003, Nat Rev Cancer, V3, P756	289	0.06	2003
10	Ridgway J, 2006, Nature, V444, P1083	283	0.07	2006

Table 4. Top 10 cocited references

path indicates that papers published in molecular/biology/immunology journals are often cited by molecular/biology/genetics journals.

#### Cocited references and reference bursts

The top 10 cocited references are shown in Table 4. We can see that the reference "Artavanis-Tsakonas S, 1999, Science, V284, P770" was the most cocited at 803 times. "Weng AP, 2004, Science, V306, P269" was cocited only 480 times, although its centrality was as high as 0.30, which shows that this reference has great influence. Figure 6A shows the network of cocited references. A citation burst is an indicator of the most active research area and represents a sudden burst that is likely to last a year or more. In other words, such a paper brings attention to the field. Figure 6B lists the top 20 references with the strongest citation bursts. The highest citation burst value (strength = 60.97) among the publications related to the Notch signaling pathway in cancer was observed for Bray F (2018), and it was effective between 2019 and 2021.

#### Keywords and keyword bursts

Keywords are the labels for an article, and the analysis of keywords can allow us to quickly understand the theme of the article and grasp the research hotspots and research frontiers in this field. The top 20 keywords that appeared frequently in articles related to the Notch signaling pathway in cancer are shown in **Table 5**. After excluding the unimportant keywords, the top 3 keywords were activation, differentiation and growth, indicating that these areas are research hotspots in this field. Figure 7A shows the clustering analysis of the keywords. As shown in the figure, the 4 different colors red, blue, yellow and green represent different areas of research. The keywords in the red clusters include apoptosis, proliferation, and resistance; those in the blue clusters include cancer stem cells, progenitor cells, and identification; those in the green clusters include c-myc, p53, and pathways; and those in the yellow clusters include vascular endothelial growth factor (VEGF), growth factor, and tumor growth. Figure 7B shows the change in keywords over time, which can provide a more intuitive understanding of the latest research hotspots.

Keyword bursts can be used to analyze the research frontiers in a certain field. **Figure 8** lists the top 20 keywords with the strongest citation bursts. As seen from the figure, the keywords that are still in the burst stage as of 2021 are metastasis, mechanism, epithelial-mesenchymal transition (EMT), invasion, target and resistance, indicating that these keywords are the research frontiers in this field.

#### Discussion

In this study, we performed a bibliometric analysis of 6494 studies related to the Notch signaling pathway in cancer in the WoSCC. We used Microsoft Excel 2020, CiteSpace V and VOSviewer to cluster and visualize the collected data to learn about the research output, research hotspots, and research frontiers in this field, thus providing guidance for basic and

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#### **Top 20 References with the Strongest Citation Bursts**

References	Year	Strength	Begin	End	2001 - 2021
Artavanis-Tsakonas S, 1999, SCIENCE, V284, P770, DOI 10.1126/science.284.5415.770, DOI	1999	31.36	2001	2004	
Radtke F, 2003, NAT REV CANCER, V3, P756, DOI 10.1038/nrc1186, DOI	2003	30.65	2004	2008	
Weng AP, 2004, SCIENCE, V306, P269, DOI 10.1126/science.1102160, DOI	2004	40.62	2005	2009	
van Es JH, 2005, NATURE, V435, P959, DOI 10.1038/nature03659, DOI	2005	29.82	2006	2010	
Noguera-Troise I, 2006, NATURE, V444, P1032, DOI 10.1038/nature05355, DOI	2006	38.2	2008	2011	
Bray SJ, 2006, NAT REV MOL CELL BIO, V7, P678, DOI 10.1038/nrm2009, DOI	2006	35.74	2008	2011	
Hellstrom M, 2007, NATURE, V445, P776, DOI 10.1038/nature05571, DOI	2007	34.43	2008	2012	
Ridgway J, 2006, NATURE, V444, P1083, DOI 10.1038/nature05313, DOI	2006	33.29	2008	2011	
Kopan R, 2009, CELL, V137, P216, DOI 10.1016/j.cell.2009.03.045, DOI	2009	55.7	2010	2014	
Ranganathan P, 2011, NAT REV CANCER, V11, P338, DOI 10.1038/nrc3035, DOI	2011	41.82	2012	2016	
Agrawal N, 2011, SCIENCE, V333, P1154, DOI 10.1126/science.1206923, DOI	2011	30	2013	2016	
Stransky N, 2011, SCIENCE, V333, P1157, DOI 10.1126/science.1208130, DOI	2011	29.51	2013	2016	
Siegel R, 2014, CA-CANCER J CLIN, V64, P9	2014	33.29	2015	2017	
Andersson ER, 2014, NAT REV DRUG DISCOV, V13, P359, DOI 10.1038/nrd4252, DOI	2014	32.87	2015	2019	
Takebe N, 2014, PHARMACOL THERAPEUT, V141, P140, DOI 10.1016/j.pharmthera.2013.09.005, DOI	2014	27.66	2015	2018	
Torre LA, 2015, CA-CANCER J CLIN, V65, P87, DOI 10.3322/caac.21262, DOI	2015	30.22	2016	2019	
Takebe N, 2015, NAT REV CLIN ONCOL, V12, P445, DOI 10.1038/nrclinonc.2015.61, DOI	2015	43.78	2017	2021	
Aster JC, 2017, ANNU REV PATHOL-MECH, V12, P245, DOI 10.1146/annurev-pathol-052016-100127, DOI	2017	38.57	2018	2021	
Yuan X, 2015, CANCER LETT, V369, P20, DOI 10.1016/j.canlet.2015.07.048, DOI	2015	27.56	2018	2021	
Bray F, 2018, CA-CANCER J CLIN, V68, P394, DOI 10.3322/caac.21492, DOI	2018	60.97	2019	2021	

Figure 6. (A) Network of cocited references; and (B) top 20 references with the strongest citation bursts.

clinical researchers. Our results indicate that no more than 100 papers were published per year prior to 2005, indicating that research related to the Notch signaling pathway in cancer was in its infancy during this period. Since 2007, the number of papers in this field has increased at an alarming rate, indicating that this field is receiving increasing attention and

Rank	Keyword	Count	Centrality	Year
1	expression	2140	0.24	2001
2	notch	1893	0.05	2001
3	cancer	1205	0.05	2003
4	activation	1130	0.10	2001
5	differentiation	884	0.16	2001
6	growth	828	0.04	2001
7	proliferation	788	0.04	2004
8	pathway	779	0.15	2001
9	apoptosis	689	0.03	2001
10	stem-cells	558	0.03	2005
11	cells	540	0.08	2001
12	gene	482	0.15	2001
13	inhibition	481	0.01	2002
14	metastasis	460	0.00	2016
15	angiogenesis	426	0.04	2002
16	gene-expression	418	0.16	2001
17	breast-cancer	382	0.00	2012
18	survival	376	0.00	2014
19	signaling pathway	367	0.07	2004
20	identification	356	0.06	2002

**Table 5.** Top 20 keywords related to the

 Notch signaling pathway in cancer

that the related research is gradually maturing. Currently, the Notch signaling pathway has been confirmed to play a key regulatory role in multiple human cancers [17-19]. As a result, a large number of papers are produced each year, and this number will continue to grow in the coming years.

We analyzed and visualized the distribution of publications across countries and institutions, which enables us better understand which countries and institutions are the main contributors to this field. Until 2017, the USA had long been the world leader in this field, both in terms of the number and impacts of the papers published. Although China has made a late start in this field, its pace is staggering. Since 2017, China has published more papers than the USA every year, and its lead has gradually expanded. There is no doubt that China is gradually becoming one of the leaders and making outstanding contributions in this field. However, although the USA produces fewer papers per year than China, its influence in the field remains significant. Studies have shown that the development of the economy contributes to more advanced scientific research, which leads to more research output [20]. Obviously, devel-

oped countries have more money to invest in scientific research; therefore, they tend to be the major contributors to scientific research [21]. Although China is a developing country, as the world's second largest economy, it is increasingly aware of the importance of scientific research; therefore, it can make such great achievements in this field. In addition to economic level, the prevalence of English and internet penetration were also significantly correlated with a country's scientific output [22]. Mutual cooperation between countries and institutions can facilitate the progress of scientific research. The USA has exhibited extensive cooperation with other countries and has had a far-reaching impact; therefore, it has a high centrality, which can benefit China.

The author with the most published articles in this field was L Miele, whose research focused on cell differentiation, EMT and Notch signaling pathway mechanisms in different cancers [23-25]. Cocited authors are two or more authors who are cited by one or more papers at the same time, and these two or more authors constitute a cocited relationship. The most frequently cocited author was ZW Wang at 912 times. His studies mainly focused on chemotherapy resistance and cell apoptosis [26, 27]. The cocited author with the highest centrality was S Artavanis-Tsakonas. In general, a centrality of more than 0.1 means that the author is influential and representative of a particular field. Among the top 10 cocited authors, 4 authors have a centrality exceeding 0.1, indicating that these authors have a great influence on other authors. Analyzing the distribution of publications in journals can help us understand the distribution of disciplines in this field and help scholars choose more appropriate journals at submission. Papers relat ed to the Notch signaling pathway in cancer are most commonly published in journals such as PLoS One, Cancer Research and Oncotarget, which focus on oncology and biology. Among the top 10 journals in the list of cocitations, all journals have more than 5000 cocitations and 5 journals have a centrality of over 0.1, which suggest that these journals have a great influence in this field. Studies have shown that the accessibility of a journal, that is, whether the journal is open to access, is also one of the factors affecting the citation times of a journal. Therefore, it should be made clear that less cited journals are not unimportant.



Figure 7. (A) Clustering analysis of the keywords; and (B) trends of key word changes over time.

# Top 20 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2001 - 2021
receptor	2001	30.83	2001	2011	
transformation	2001	23.1	2003	2008	
c myc	2001	40.39	2005	2011	
beta catenin	2001	13.79	2005	2007	
angiogenesis	2001	29.48	2007	2016	
in vivo	2001	28.29	2008	2015	
growth factor	2001	16.36	2009	2010	
acute lymphoblastic leukemia	2001	16.24	2010	2011	
inhibits tumor growth	2001	17.93	2011	2012	
progenitor cell	2001	16.38	2012	2013	
breast cancer	2001	15.73	2014	2017	
epithelial mesenchymal transition	2001	24.39	2015	2018	
metastasis	2001	33.89	2016	2021	
carcinoma	2001	16.78	2017	2018	
therapy	2001	16.37	2017	2018	
mechanism	2001	16.83	2018	2021	
emt	2001	25.39	2019	2021	
invasion	2001	24.51	2019	2021	
target	2001	18.44	2019	2021	
resistance	2001	14.58	2019	2021	

Figure 8. Top 20 keywords with the strongest citation bursts.

Among the most frequently cocited references related to the Notch signaling pathway in cancer was a paper published in Science in 1999, which reviewed the elements and functions of the Notch signaling pathway [28]. The cocited reference with the highest centrality was published in Science in 2004, and it provides a strong rationale for targeted therapies that interfere with the Notch signaling pathway and has thus been widely cited by other scholars [29]. From the top 20 references with the strongest citation bursts, the paper that received the most attention in the last 3 years was published in Ca-A Cancer Journal For Clinicians by F Bray et al., who counted the incidence and mortality worldwide for 36 cancers in 185 countries [30]. There is no doubt that the above three references provide an important foundation for the development of this field and are of great significance.

To understand the research hotspots and frontiers in this field, we visualized the keywords. After excluding the unimportant keywords, the top 3 keywords were activation, differentiation and growth, indicating that these topics are research hotspots in this field. As reported in the literature, the activation of the Notch signaling pathway can regulate the occurrence and progression of various cancers, such as esophageal cancer, rectal cancer and lung cancer [31-33]. This topic has long been a research hotspot in this field. Furthermore, multiple studies have shown that Notch signaling is also closely related to tumor cell differentiation and tumor growth [34, 35]. Due to the different research hotspots in different periods, we analyzed the trend of keywords changing over time. During 2013 and 2014, the research hotspots were mainly focused on Drosophila, genes and transcription. During 2015 and 2016, the research hotspots shifted to apoptosis, activation, growth and other aspects. With the passage of time, research hotspots now mainly focus on therapy, resistance, metastasis, and progression. In terms of keyword bursts, scholars have focused on metastasis, mechanism, EMT, invasion, target and resistance, indicating that these keywords are the research frontiers in this field. The role of the Notch signaling pathway in tumor metastasis and invasion is already well established and has been demonstrated by multiple studies [36, 37]. The Notch signaling pathway can reverse and prevent EMT, which provides new ideas for the treatment of various cancers [38, 39]. Chemotherapy and immunotherapy resistance have long been considered a challenging problem. Therefore, finding more effective targets to solve this problem is urgent. Dysregulation of the Notch signaling pathway is one of the key factors for drug resistance in various tumors, and it is also a topic with the closest clinical relevance. Studies have shown that activation of the Notch signaling pathway can lead to drug resistance while inhibition of the Notch signaling pathway can reverse drug resistance [40-42]. Given the important role of the Notch signaling pathway in tumor resistance and its close relationship to clinical practice, this topic is the current research hotspot and frontier and will also be the main research direction of scholars around the world in the future.

Our study has the following limitations. First, we only used data from the WoSCC and did not collect data from other databases, which may have affected the research results. Second, although we have developed a rigorous retrieval strategy, we may have missed some data. Finally, the literature in the WoSCC is constantly updated over time; therefore, the retrieval results in this study may not represent the actual included literature.

## Conclusions

This study presents a bibliometric analysis of articles focused on the Notch signaling pathway in cancer from 2001 to 2021. Over the past 20 years, research in this field has been increasing continuously and explosively. As the top two major economies in the world, the USA and China have made outstanding contributions to the development of this field. At present, the research hotspots and research frontiers in this field mainly focus on the mechanism of the Notch signaling pathway in cancer and how to reverse drug resistance of cancer through the Notch signaling pathway, which will also be the research trend in this field in the future. This analysis could help researchers around the world understand the future directions of basic and clinical research in this field.

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#### Disclosure of conflict of interest

None.

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