R E V I E W

Trends in Research on the P2X7 Receptor: A Bibliometric and Visualization Analysis

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Abstract: The P2X7 receptor (P2X7R), activated by ATP, participates in mediating a variety of biological processes such as the release of inflammatory factors, thereby affecting the pathogenesis of numerous diseases. Despite its clinical significance, comprehensive bibliometric studies on P2X7R-related research remain scarce. To address this gap, we conducted a bibliometric investigation to quantify publication outputs, identify leading contributors, and map geographical distributions of P2X7R-related research, ultimately elucidating current research frontiers and emerging trends. Utilizing visualization techniques, complex bibliometric relationships were transformed into interpretable graphical representations. Our Web of Science query for "P2X7R" identified 4551 original research articles by 13,471 authors published since 1985. Publication volume demonstrated sustained growth, with China emerging as the predominant contributor in quantitative output (1871 articles) and the United States leading in international collaborations. Thematic mapping revealed two principal research areas: "P2X7R, inflammation, microglia" and "P2X7R, apoptosis, purinergic". Notably, "P2X7R, P2 receptors, oxidative stress" encompassed both motor and niche themes, thus representing the trajectory of future development potential. Through bibliometric and visualization analysis, we found that the literature related to P2X7R is on the rise and will enter a new stage of interdisciplinary integration development in the future.

Keywords: P2X7 receptor, bibliometrix, VOSviewer, web of science

Introduction

Adenosine triphosphate (ATP) was first identified half a century ago by Geoffrey Burnstock, who discovered that ATP is a neurotransmitter released by the then-termed non-adrenergic, non-cholinergic nerve endings in the intestines and bladder.[1] Extracellular ATP exerts its effects via P2 receptors found on the cell surface. P2 receptors can be divided into two families: ligand-gated ionotropic P2X receptors and G-protein-coupled P2Y receptors.[2] The P2X7 receptor (P2X7R) is a unique member of the P2X receptor family that is relatively insensitive to ATP. Furthermore, Schäfer et al reported that three high-frequency polymorphisms (H155Y, R270H, and A348T) of P2X7R could be found in various human subpopulations.[3] P2X7R is distributed across both the peripheral and central nervous systems, in which the vast majority of immune cells in the peripheral nervous system express P2X7R,[4] where it is involved in immune regulation and bone formation.[5] Moreover, the activation of this receptor has also been shown to drive tumor implantation, growth, and angiogenesis.[6] Conversely, P2X7R is richly expressed on microglia in the central nervous system (CNS),[7] where it responds to inflammatory signals by regulating the release of neurotransmitters, thereby participating in signal transduction.[8] Yin et al previously showed that the ATP-P2X7R signaling axis can serve as a potential therapeutic target for alleviating traumatic CNS injuries and related complications.[9] Furthermore, Jiang et al demonstrated that the activation of P2X7R can increase the number of cathepsin L (CTSL)-containing exosomes, which is

6349

associated with the pathogenesis of Parkinson's disease.[8] In addition, Ren et al found that neuroinflammation mediated by microglial P2X7R in the olfactory bulb was implicated in the pathogenesis of olfactory dysfunction in a mouse model of allergic rhinitis.[10] A subsequent study further revealed that P2X7R was associated with depressive-like behaviors in mice with allergic rhinitis, and that such behaviors were mitigated by treatment with a P2X7R inhibitor.[11] All of these prior studies indicate that P2X7R antagonists could serve as a potential therapeutic strategies for Parkinson's disease, olfactory dysfunction associated with allergic rhinitis, and depression.

Although numerous studies have been conducted on the physiological and pathological aspects of P2X7R, as yet there have been no bibliometric studies on P2X7R-related research. To address this knowledge gap, in this bibliometric study, we examined the overall article information and relevant authors and keywords, in order to clarify the distribution of articles with respect to their publication, country, and authors, thereby allowing us to gain a better understanding of the data fluctuations in recent years. In addition, zones based on Bradford's law were applied to illustrate the distribution of major journals, whereas thematic maps and visual analysis were employed to identify the themes and keywords. These findings should enable researchers or clinicians to gain a more comprehensive and accurate understanding of P2X7R, thus providing new ideas for future research related to P2X7R.

Materials and Methods
Data Sources and Literature Search

Data for this quantitative analysis were extracted from the Web of Science Core Collection (WOSCC), a standard database widely used in academia that encompasses more than 12,000 academic journals.[12] Retrieve from this database, focusing on the topic of P2X7R, using the search field "Title-abstract- keyword". The following search formula, in which TS indicates the topic, AB the abstract, and AK the author keywords, was employed: ((TS=(P2X7 receptor)) OR AB=(P2X7 receptor)) OR AK=(P2X7 receptor), in order to retrieve all articles related to "P2X7R" in the database since its establishment (1985–2024). Database search revealed that the earliest article was published in 1996. 4551 articles were retrieved, and we accepted only original research articles published in English language, and screened them according to three exclusion criteria. As of April 2024, a total of 3080 relevant articles were screened. Figure 1 shows the flow diagram created according to reference.[13]
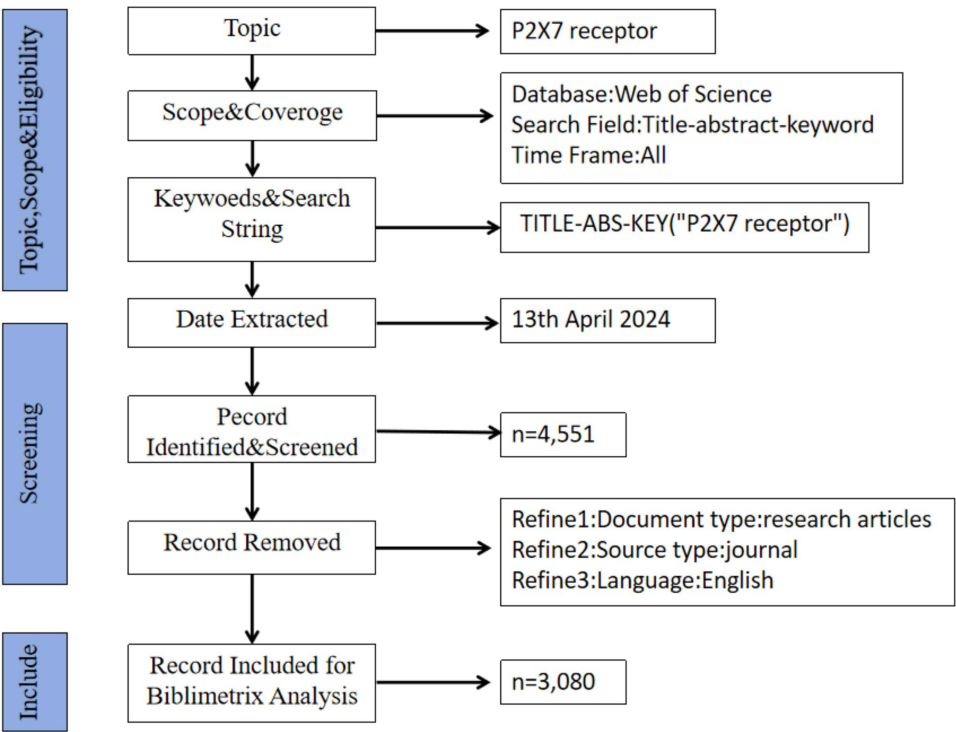

Figure 1 The flow diagram.

Data Analysis and Visualization

Using the R-supported[14] bibliometrix (version 4.3.3) and VOSviewer (version 1.6.20) software tools, bibliometric analysis was performed on all the articles that met the inclusion criteria. The number of publications by year, journal, author, and high-frequency keywords were quantified and ranked using bibliometrix (an R-Tool of R-Studio).[15] VOSviewer was applied to display the frequency of keywords, and its embedded clustering algorithm was employed to construct and visualize the co-occurrence network of keywords in the scientific literature.[16] On the basis of these bibliometric techniques, we attempted to gain a comprehensive and quantitative understanding of the literature related to P2X7R. Our analysis incorporated both numerical data and patterns, capitalizing on their advantages to establish a method for the systematic review of P2X7R. This approach allowed us to more intuitively reflect the changes in the distribution of authors and publications, thus supplementing and improving upon general systematic reviews, and to conduct a clear and structured analysis of the existing literature on P2X7R. Bibliometrics and visualization analysis use "data-driven+visual presentation" to make implicit knowledge explicit, helping researchers grasp the trends of scientific development. This approach can serve not only as a tool for research efficiency, but also as a catalyst for promoting interdisciplinary research, innovation breakthroughs, and scientific decision-making.

Results

Basic Information

Our analysis revealed a total of 5202 author keywords, with an annual growth rate of 15.61%. There were 31 authors with single-authored articles, while the percentage of internationally co-authored articles was 26.98%, and the average number of co-authors was 7.37 per paper.

Distribution of Publication years

Figure 2 shows the distribution of publication years from 1996 to 2024. The first article to mention "P2X7R" was "Purines and cell death" by Claudio Franceschi, published in the journal DRUG DEVELOPMENT RESEARCH.[17] The academic community subsequently continued to explore P2X7R, with the annual publication output showing an overall trend of gradual increase. The article with the highest number of citations worldwide was "Pannexin-1 mediates large pore formation and interleukin-1β release by the ATP-gated P2X7 receptor" by Pablo Pelegrin, published in EMBO JOURNAL.[18]
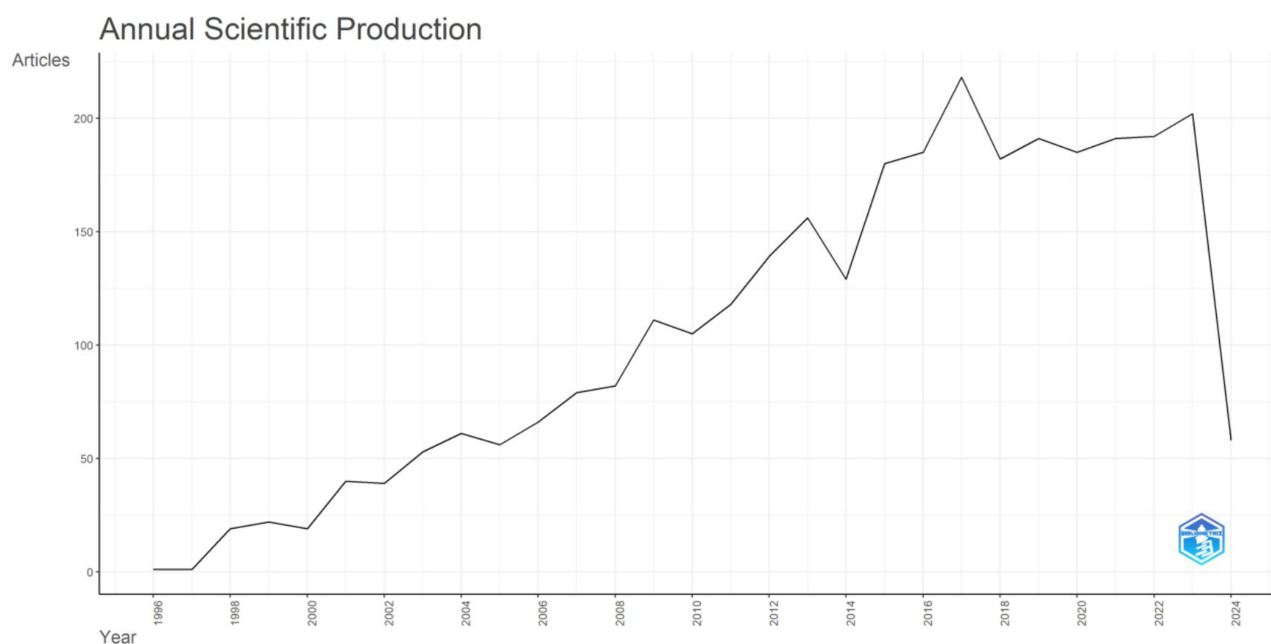

Figure 2 Distribution of publication years constructed using bibliometrix.

Distribution of Publications by Country

Table 1 lists the top 10 countries with the highest publication output. The country with the highest number of publications was China (n=1871), followed by the United States (n=1821), Brazil (n=811), and Italy (n=723). Interestingly, the national publication line charts shown in Figure 3 indicate that, prior to 2023, the United States took the lead by far in terms of publication output, but was surpassed by China thereafter.

As shown in the visualization analysis (Figure 4), China and the United States were the largest clusters on the map, with close collaborations between the two. However, the United States had closer links with other national clusters than China did.

Distribution of Publications by Journal

A total of 3080 articles published in 761 journals were included in this study. On the basis of Bradford's law, the articles published in these journals were divided into three zones, as shown in Table 2. Zone 1 included 21 core journals, with 1027 publications, and zone 2 included 112 core journals, with 1040 publications. Table 3 lists the top 10 journals with the highest number of publications. The journal with the most publications was PURINERGIC SIGNALLING (127 articles), which focuses on the field of purinergic signal transduction. This was followed by the JOURNAL OF IMMUNOLOGY (94 articles), and PLOS ONE (74 articles). In general, the majority of journals focused on topics in the fields of immunology and biochemistry, with a minority covering topics in pharmacology and neurology.

Distribution of Publications by the Most Relevant Authors

Among the included studies, a total of 13,471 authors were involved in writing articles related to "P2X7R", of whom only 31 were single authors, and the remaining were co-authors. As shown in Table 4, the top author was Di Virgilio F, who published 95 articles as the lead author and had the highest number of citations. The second author was Coutinho-Silva R, with 81 relevant articles. As shown in Figure 5, Di Virgilio F is a leading author in this research field, with his relevant publications showing a very high frequency and correlation.

Keyword Analysis

A search of all the articles that met the inclusion criteria revealed that, in addition to "P2X7R", high-frequency author keywords included "ATP", "Inflammation", and "Microglia". From this analysis, we constructed a thematic map based on the author keywords to display the current popular or clustered themes,[19] thus highlighting their development degree and relevance degree. This map was divided into four zones, as shown in Figure 6. The vertical axis represents the

Table 1 Ranking of Publication Output by Country

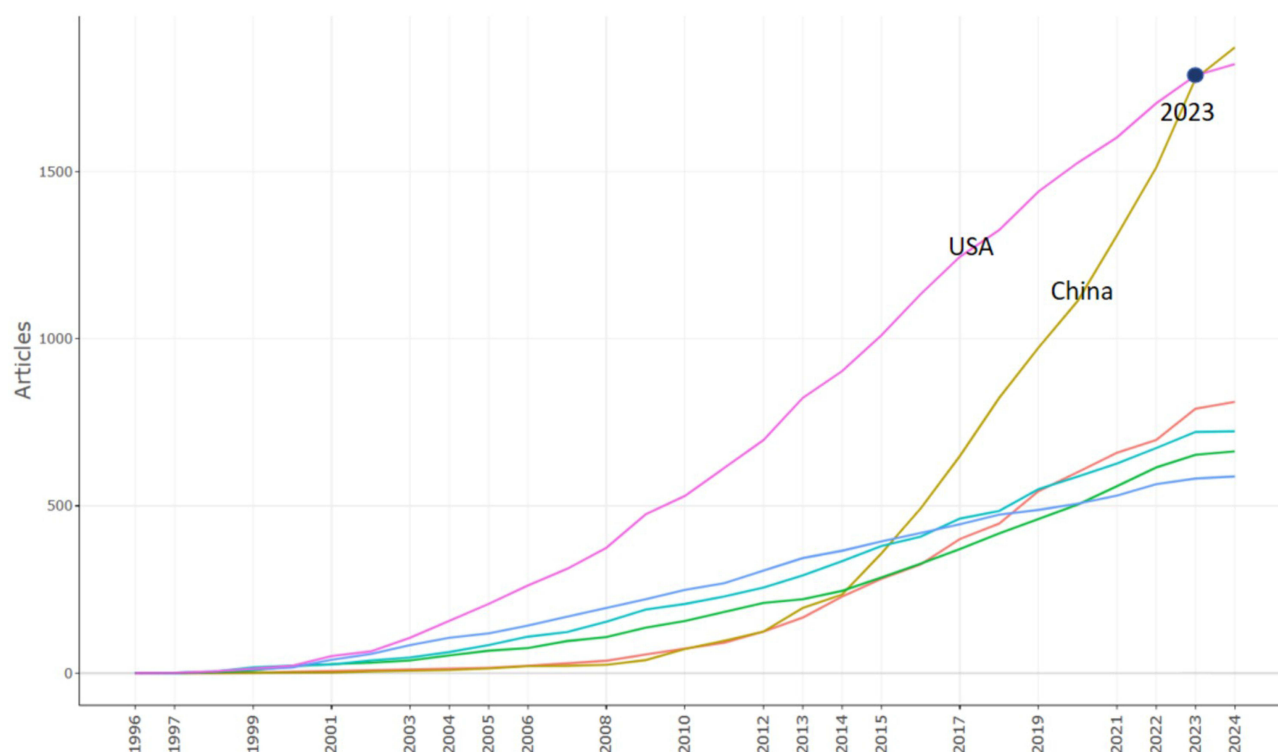|	Region	Frequency
1	CHINA	1871
2	USA	1821
3	BRAZIL	811
4	ITALY	723
5	GERMANY	663
6	UK	588
7	AUSTRALIA	523
8	JAPAN	516
9	FRANCE	416
10	SPAIN	344

Figure 3 Distribution map of the year of publication by country constructed using bibliometrix.

development degree, while the horizontal axis represents the relevance degree. The relevance degree reflects the interconnectivity between different themes, and the development degree reflects the extent to which a given theme has been developed.

Figure 6 shows the thematic mapping of high-frequency author keywords in P2X7R research. A total of seven clusters emerged, from which the top three terms formed one cluster. According to current statistics, there were no clusters in the upper right quadrant, which suggests a lack of clear motor themes. Motor themes can drive further exploration in future research, and constitute an important part of the development in this field. The lower right quadrant includes the basic themes, illustrating the most fundamental and core themes of the field, with strong relevance and high development. For example, the two clusters, "P2X7R, inflammation, microglia" and "P2X7R, apoptosis, purinergic" were identified as fundamental research topics that have garnered the interest of numerous authors. The lower left quadrant encompasses emerging or declining themes, with relatively low relevance and development degree. "Pannexin" is included in this cluster, indicating that this research hotspot is emerging or declining. The upper left quadrant includes niche themes, which are characterized by high development degrees, but low relevance degrees. The thematic map also revealed two thematic clusters covering multiple quadrants. The "ATP, P2X7R, purinergic receptors" cluster encompassed basic themes and motor themes, indicating that it is not only a core area in this field but also has some impact on future themes. Furthermore, the "P2X7R, P2 receptors, oxidative stress" cluster combined niche themes and motor themes, indicating a high development degree, thus suggesting a significant potential and opportunity to develop into a research hotspot.

By employing VOSviewer, we extracted words that appeared at least 15 times from the title and abstract of each article for a word co-occurrence analysis. From this, a network connection diagram was generated, with different colors used to represent different word clusters. This map reflected the main trends of big data articles and their mutual relationships. In Figure 7, words that are closer together are more strongly correlated, whereas the size of the circle represents the frequency of the words.[20] In Figure 8, the diagram is marked with time nodes to show the trend of words over time, with different colors representing different time periods. The color changes from blue to yellow, and the closer
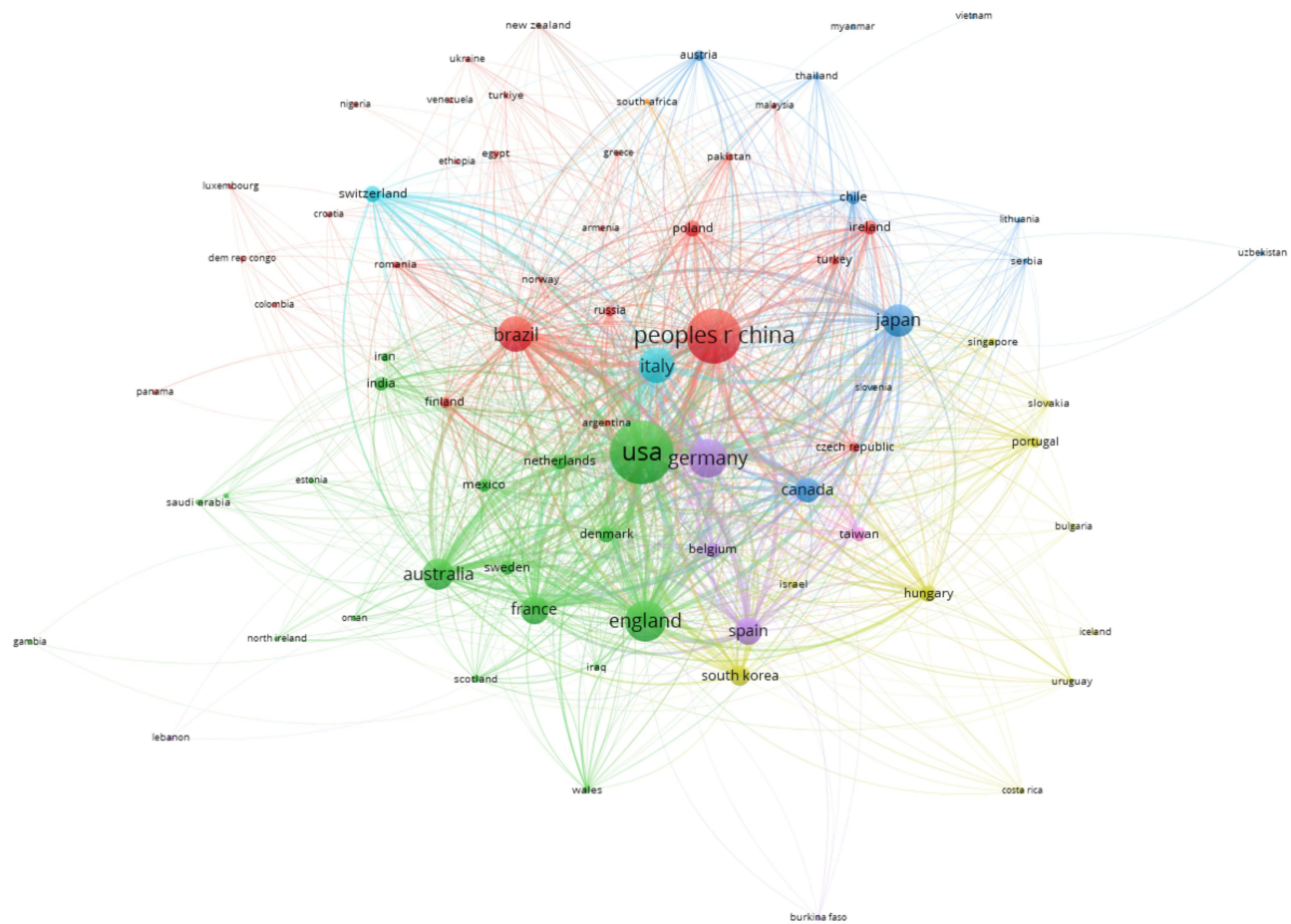
Figure 4 National document cluster map constructed using VOSviewer (China and the United States are shown in red and green, respectively).

it is to yellow, the more it reflects the recent research core content. The closer it is to blue, the earlier it appears, indicating the most core basic vocabulary in the field that has been around in the past.

Discussion

P2X7R is a trimeric ion channel gated by extracellular ATP. It has been detected in an increasing number of different cell types, including stem cells, blood cells, glial cells, neurons, ocular cells, osteocytes, dental cells, exocrine cells, endothelial cells, muscle cells, kidney cells, and skin cells.[21] Based on bibliometric analysis, we comprehensively summarized the existing research on P2X7R from 1985 to 2024; intuitively presented an overview of international research on P2X7R published in the past 30 years; and pieced together a basic picture of its research hotspots, frontiers, and trends. Our findings further revealed that since the first relevant article was published in 1996,[17] the number of publications in this field has been gradually increasing. Specifically, Burnstock G's definition of the concept of purinergic signaling sparked significant controversy within the academic community, which led to a long period of

Table 2 Ranking of Publication Output by Journal (Classified by Zones in Bradford's Law)

Zone	Number of Publications	Number of Journals	Percentage of Journals
1	1027	21	2.7
2	1040	112	14.7
3	1013	628	82.5

Table 3 Top 10 Journals by Publication Output

Rank	Sources	Articles
1	PURINERGIC SIGNALLING	127
2	JOURNAL OF IMMUNOLOGY	94
3	PLOS ONE	74
4	JOURNAL OF BIOLOGICAL CHEMISTRY	73
5	INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	64
6	BRITISH JOURNAL OF PHARMACOLOGY	59
7	SCIENTIFIC REPORTS	49
8	JOURNAL OF NEUROSCIENCE	45
9	FRONTIERS IN PHARMACOLOGY	44
10	FRONTIERS IN IMMUNOLOGY	42

Table 4 Top 10 Most Relevant Authors and Associated Local Citation Statistics

	Authors	Articles	Articles Fractionalized	Local Citations
1	DI VIRGILIO F	95	14.30	2087
2	COUTINHO-SILVA R	81	11.84	813
3	SLUYTER R	59	12.98	1314
4	WILEY JS	57	10.13	1773
5	KOCH-NOLTE F	46	5.25	635
6	FALZONI S	40	5.43	1071
7	MIRAS-PORTUGAL MT	38	5.90	921
8	BHATTACHARYA A	35	4.15	528
9	BURNSTOCK G	34	7.16	574
10	LIANG SD	33	2.20	171

in-depth research on this issue. As P2X7R is a member of the purinergic receptor family,[2] subsequent research has shown that P2X7R plays a key role in a number of CNS diseases. Our study also identified prominent research areas and predicted research directions, with the aim of providing valuable insights and suggestions for future investigations in the field of P2X7R.

Analysis of Publications by Country

Based on our statistical analysis outlined above, we concluded that China and the United States were the two dominant countries with respect to cumulative publication output. Prior to 2023, the United States was consistently the frontrunner in terms of research output due to its position as a global leader in economy and power. This finding has been corroborated by previous studies.[22] However, China's publication output showed a significant increasing trend, even surpassing that of the United States in 2023. The main reason for this can be traced to China's rapidly advancing economy and comprehensive power in recent years. Thus, the increase in publication output can be attributed to the increase in research funding, economic stability, and research infrastructure.[23] This may also be related to the growing
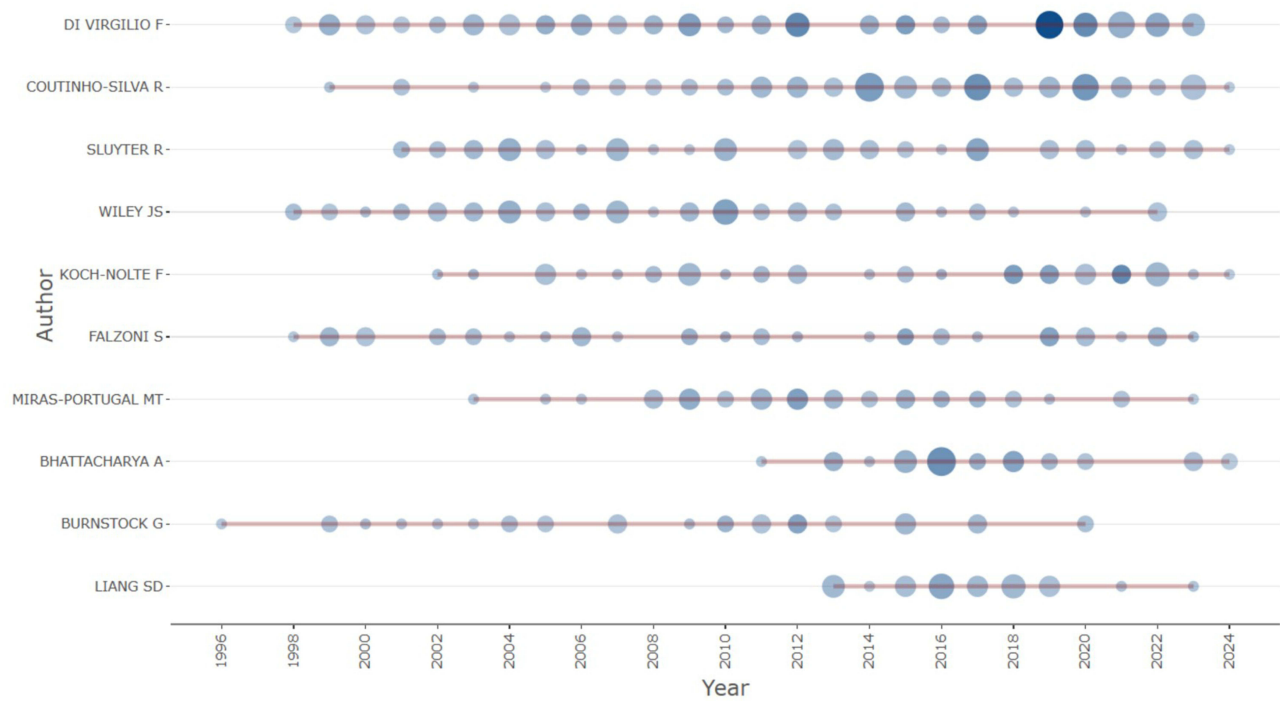
Figure 5 VOSviewer analysis of the author's publication frequency and correlation, in which the size of the circle represents the frequency of publication in a year, and the strength represents the correlation.
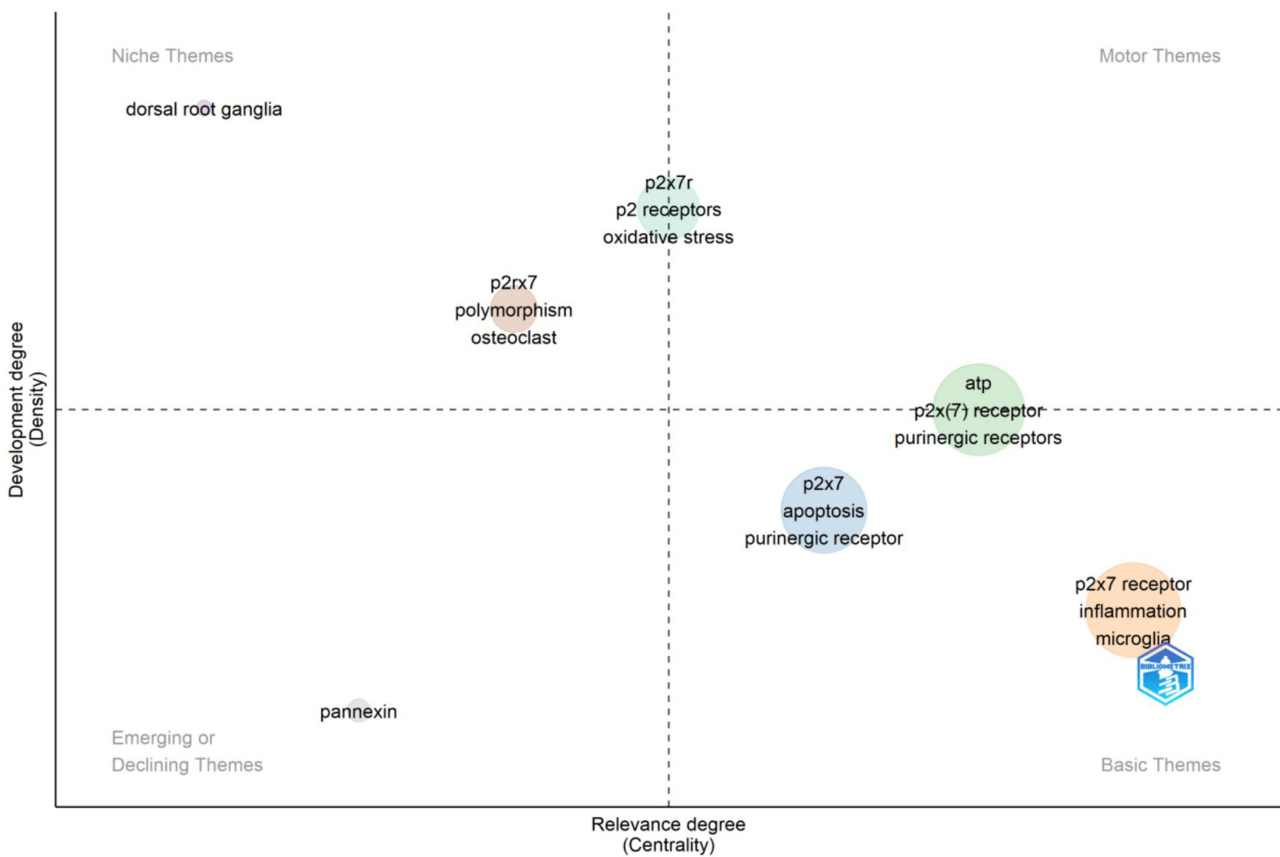

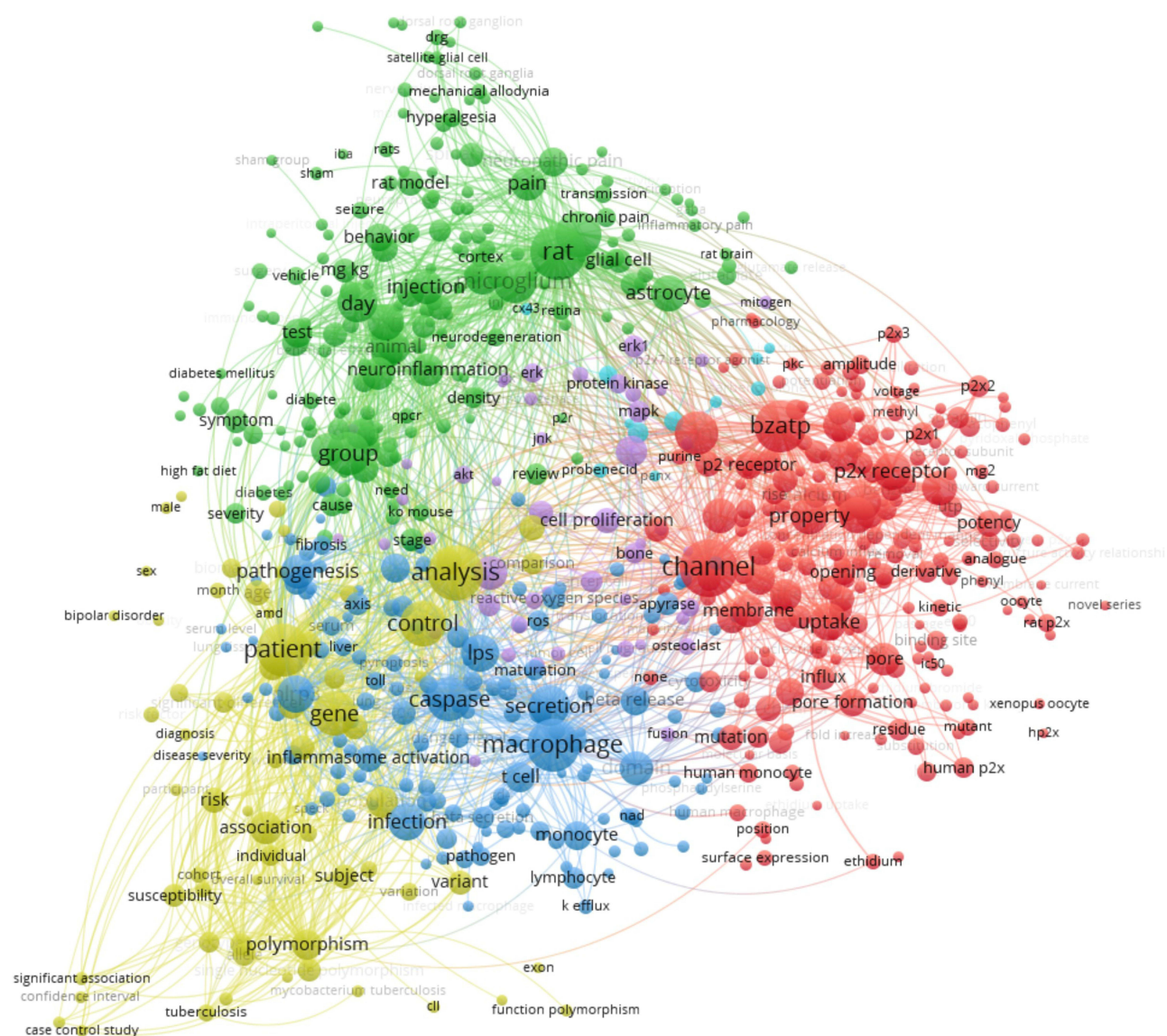**Figure 6** Bibliometrix analysis of thematic maps relating to P2X7 receptors.

Figure 7 VOSviewer analysis of co-occurrence diagram of words related to P2X7.

population of patients with neurological disorders[24] as well as the increasing demand for pain relief, which has contributed to an increase in relevant research. An evaluation of the degree of international exchange through the density of cooperation networks in Figure 4 revealed that the United States exhibits a greater density of cooperation networks and closer international exchanges. This closeness is not only a natural result of its historical traditions and multiculturalism, but also actively driven by global competition, educational strategies,[25] and ideological exports. Although China had a high number of publications, it did not show close collaborations with other countries, indicating limited cooperation with other regions. Through this cross regional cooperation, it can be seen that China still focuses on domestic cooperation in this field, and international cooperation needs to be strengthened.

Analysis of Publications by Journal

PURINERGIC SIGNALLING was identified as the journal with the most publications. This journal focuses on the study of purinergic signaling, covering the molecular mechanisms, physiological and pathological effects, and therapeutic applications of purine receptors (including the P2X and P2Y families). As an important member of the purine receptor family, the P2X7 receptor has naturally become one of the core themes of this journal. The annual publication volume of
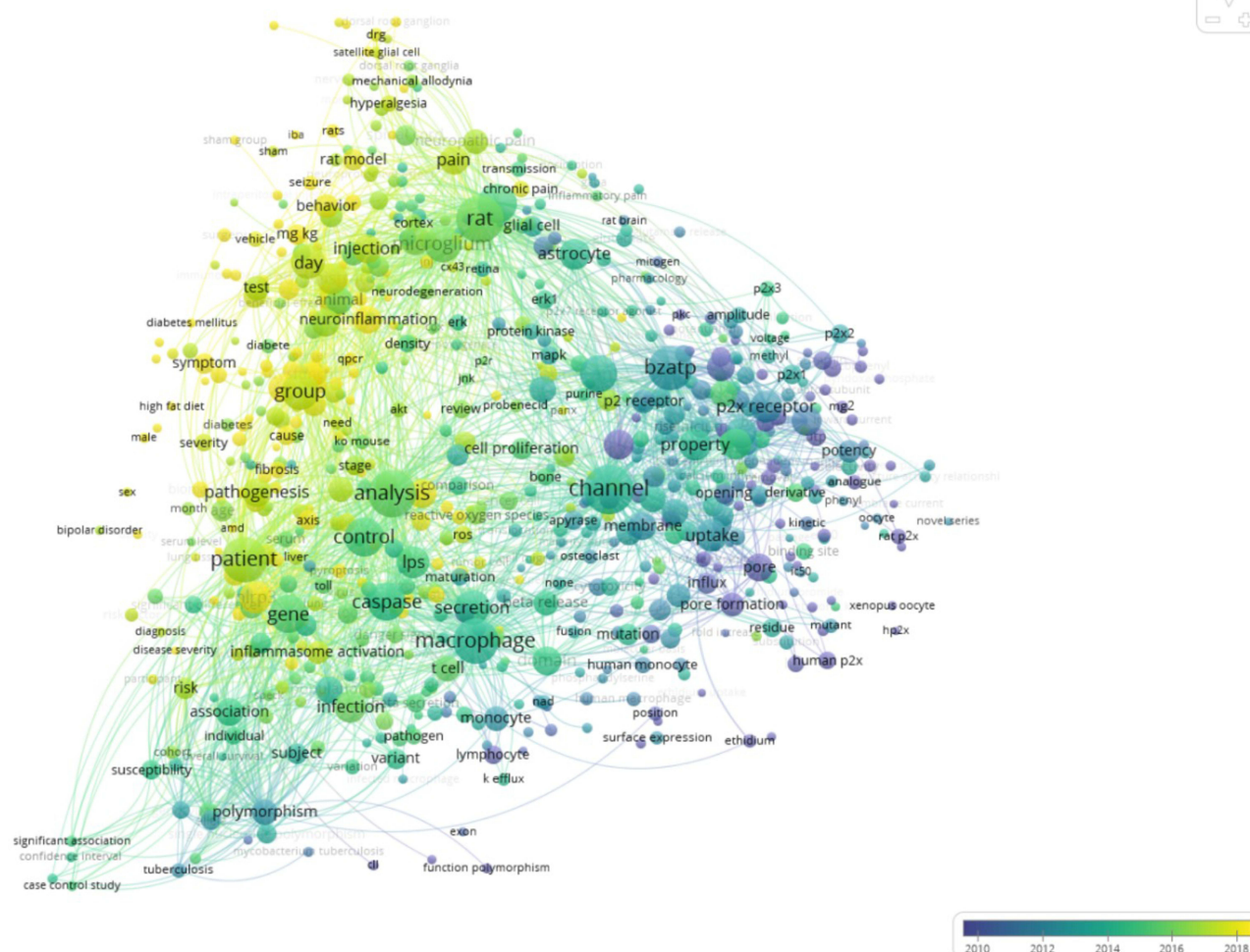
Figure 8 VOSviewer analysis of word co-occurrence time analysis graph related to P2X7.

this journal is approximately 58 articles, 75.86% of which are research-oriented, and many involve functional research on P2X7 receptors (such as pain regulation, inflammatory response, etc)., making it a centralized publishing platform in this field.[26] In addition, the H-index of the journal is 52, indicating that its published P2X7R related literature has high academic influence. The JOURNAL OF IMMUNOLOGY, which focuses mainly on research related to clinical immunology, was the second most prolific journal, followed by PLOS ONE, a comprehensive journal with a broader content range. The second ranked journal, although authoritative in immunology, has a wider coverage, including innate and adaptive immunity, inflammation, infection, etc. P2X7R has been studied only as a part of immune regulation mechanisms, with more diverse topics. In terms of research depth and influence, PURINERGIC SIGNALLING is more systematic, covering molecular mechanisms, disease models (such as epilepsy and breast cancer) and verification of therapeutic targets.[27–29] The research on JOURNAL OF IMMUNOLOGY mostly focuses on immune regulatory fragments and lacks interdisciplinary integration. In summary, the disciplinary focus, relevant publication volume, and academic influence of the journal collectively make PURINERGIC SIGNALLING the core publishing platform for P2X7R research. A comparison of these findings clearly reveals that strengthening the interdisciplinary research between purinergic signaling and neuroscience, immunology, inflammation, and pain is the key to increasing the publication volume of P2X7R.Interdisciplinary collaboration and exchange can even become a norm in P2X7R.

Research Hotspots and Frontiers

Our results showed that the most cited article was "Pannexin-1 mediates large pore formation and interleukin-1β release by the ATP-gated P2X7 receptor",[18] which was published in 2006 and was not the first article to introduce P2X7R. These findings suggest that the emergence of P2X7R has not attracted significant attention. Instead, this article was widely cited after it was published, as it focused on the relationship between pannexin-1 (a mammalian protein) and P2X7R, with results showing that pannexin-1 is an upstream molecule that can induce inflammasome activation through P2X7R. Subsequent articles also focused on the keyword "pannexin-1", and the author himself also cited this article in a later updated paper introducing the association between P2X7R-pannexin and IL-1β release.[30]

According to the thematic map, the most common basic keywords were clustered around "microglia" and "inflammation". In this context, one study investigating the expression of P2X7R in the brain detected its presence on microglia in the CNS.[31] Subsequently, several articles on microglia gradually emerged. For example, Yiangou et al demonstrated that P2X7R was associated with increased microglial immunoreactivity, following COX-2 and CB2 activation in multiple sclerosis.[32] In addition, the word "inflammation" was found to be closely associated with "nerves" in studies using mouse models, while the nodes of this cluster were closely connected in the visualization analysis diagram. A white-yellow-green color pattern was also used to illustrate the changes in word frequency, in order to clearly distinguish the changes in words over time. These keywords began to appear with high frequency around 2016. In 2022–2023, the frequency of "COVID-19" increased due to the global outbreak of the COVID-19 pandemic, resulting in the publication of many related articles. Some researchers found that COVID-19 was associated with relevant neurodegenerative disorders. Furthermore, research showed that the activation of P2X7R led to the activation of NLPR3, which affected the onset and treatment of COVID-19, and rendered patients with neurodegenerative disorders more susceptible to infection.[33] Epilepsy is a common chronic neurological disease that can be induced and aggravated by infection with SARS-CoV-2. Research has shown that P2X7R can be activated by this virus, subsequently resulting in the exacerbation of epileptic seizures.[34] The pathogenesis of COVID-19 is thought to be closely related to the cytokine storm it triggers,[35] while the ability of P2X7R to regulate elevated inflammatory responses indicates that the purinergic system could serve as a treatment strategy to counteract cytokine storms. Moreover, this receptor can also exacerbate the immune response, while P2X7R inhibitors have been proposed as candidates for the pharmacological treatment of COVID-19 infection.[36] This demonstrates that the research trends related to P2X7R may vary according to current societal developments and public health changes, and can be affected by public health events.

The thematic mapping of keywords revealed that the two clusters, "P2X7R, inflammation, microglia" and "P2X7R, apoptosis, purinergic" are currently the most fundamental core themes. Although the "P2X7R, P2 receptors, oxidative stress" cluster currently remains a niche theme, it has a high development degree, indicating that its potential for future research and development may contribute to innovative explorations for current keywords, including "inflammation", "microglia", "apoptosis", and "purinergic".

In summary, rapid advances are being made in the field of P2X7R, and there is a growing expectation that P2X7R could be targeted to induce various downstream events, including inflammatory mediators in the development of pain,[37] cell proliferation and death, metabolic events, and phagocytosis.[21] In addition, P2X7R has been identified as a promoter of cancer cell growth,[38] which could promote the investigation of innovative therapeutic approaches targeting P2X7R-related diseases in future clinical research. For example, the inhibition of P2X7R activation is expected to serve as a potential target for pain relief and the treatment of diseases such as cancer. Nevertheless, a deeper understanding of the structure and associated signaling mechanisms of this receptor is needed to facilitate the further development of effective therapies. Furthermore, the next phase of research should involve extensive international collaboration, in order to provide new insights and directions for the continued exploration and development of P2X7R research.

Limitations

Bibliometric analysis is an important means through which research development trajectories can be developed through the identification of prominent research areas in the field related to P2X7R. However, it is important to acknowledge that this approach is not without its limitations. First, our reliance on the WOSCC database to retrieve literature information may have led

to the exclusion of relevant data contained within alternative databases. Second, despite the double-checking measures adopted, there is still a need for the manual correction of duplicate or inaccurate elements. Third, the limitations of bibliometric algorithms themselves can cause the contributions of emerging researchers to be overlooked, while the information bias between different measurement software programs can lead to inconsistent results. Finally, only articles published in English were included in this study, and those published in other languages were not analyzed. Furthermore, only high-frequency words were selected, which may have led to the loss of certain essential low-frequency words. In terms of article types, in order maintain the integrity and formality of the listed articles, we only selected original articles and excluded review articles, which may have resulted in the omission of certain representative papers.

Conclusion

In the present study, we employed bibliometrics and visualization techniques to analyze the literature related to the topic of "P2X7R" over the past 30 years, as well as to comprehensively observe the trend changes in this field based on the distribution of data by country, journal, author, and keywords. Through bibliometric data analysis, it was found that the most influential journals are PURINERGIC SIGNALLING and JOURNAL OF IMMUNOLOGY, and Di Virgilio F is the most authoritative author in the P2X7R related field. Through high-impact journals, it was found that the core of the literature related to P2X7R lies in cross collaboration with neuroscience, immunology, and pain. "Neuroinflammation" and "microglia" are both research hotspots in this field, whereas "oxidative stress" appears to be an important direction of future research. We also performed a detailed analysis and review of keywords related to "pannexin-1" and "COVID-19". Overall, the discovery of these keywords can provide researchers with a comprehensive overview of the P2X7R pattern, guide potential collaborations, and determine future research directions for P2X7R that will continue to be based on molecular biology, with interdisciplinary extensions in neurology, immunology, and pharmacology. The combination of bibliometrics and visual analysis has improved the research efficiency of scholars around the world, quickly extracting valuable information to assist scientific decision-making. It not only provides sufficient information and future development trends of P2X7R, but also builds closer academic exchanges that contribute to future academic cross fusion. The research on P2X7R shows a trend of interdisciplinary collaboration and development. In addition to the in-depth interpretation of its molecular mechanisms and signaling pathways, there will be more clinical application explorations in cross disease models such as inflammatory diseases, immune regulation, and neurological diseases in the future. Through interdisciplinary collaboration and technological innovation, the comprehensive transformation from basic research to clinical applications can be promoted.

Data Sharing Statement

No datasets were generated or analyzed during the current study. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

All authors made significant contributions to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflict of interest to report.

References

1. Burnstock G. Purinergic nerves. *Pharmacol Rev.* 1972;24(3):509–581. doi:10.1016/S0031-6997(25)06930-3
2. Burnstock G. Purinergic signalling: past, present and future. *Braz J Med Biol Res.* 2009;42(1):3–8. doi:10.1590/s0100-879x2008005000037
3. Schäfer W, Stähler T, Pinto Espinoza C, et al. Origin, distribution, and function of three frequent coding polymorphisms in the gene for the human P2X7 ion channel. *Front Pharmacol.* 2022;18(13):1033135. doi:10.3389/fphar.2022.1033135
4. Bartlett R, Stokes L, Sluyter R. The P2X7 receptor channel: recent developments and the use of P2X7 antagonists in models of disease. *Pharmacol Rev.* 2014;66(3):638–675. doi:10.1124/pr.113.008003
5. Zeng D, Yao P, Zhao H. P2X7, a critical regulator and potential target for bone and joint diseases. *J Cell Physiol.* 2019;234(3):2095–2103. doi:10.1002/jcp.27544
6. Adinolfi E, Raffaghello L, Giuliani AL, et al. Expression of P2X7 receptor increases in vivo tumor growth. *Cancer Res.* 2012;72(12):2957–2969. doi:10.1158/0008-5472.CAN-11-1947
7. Di Virgilio F, Sanz JM, Chiozzi P, et al. The P2Z/P2X7 receptor of microglial cells: a novel immunomodulatory receptor. *Prog Brain Res.* 1999;120:355–368. doi:10.1016/s0079-6123(08)63569-4
8. Jiang T, Xu C, Gao S, et al. Cathepsin L-containing exosomes from α-synuclein-activated microglia induce neurotoxicity through the P2X7 receptor. *NPJ Parkinsons Dis.* 2022;8(1):127. doi:10.1038/s41531-022-00394-9
9. Yin Y, Wei L, Caseley EA, et al. Leveraging the ATP-P2X7 receptor signalling axis to alleviate traumatic CNS damage and related complications. *Med Res Rev.* 2023;43(5):1346–1373. doi:10.1002/med.21952
10. Ren C, Mou YK, Song XY, et al. P2X7 receptor of microglia in olfactory bulb mediates the pathogenesis of olfactory dysfunction in a mouse model of allergic rhinitis. *FASEB J.* 2023;37(6):e22955. doi:10.1096/fj.202300160RR
11. Mou Y, Sun C, Wei S, et al. P2X7 receptor of olfactory bulb microglia plays a pathogenic role in stress-related depression in mice with allergic rhinitis. *Neurobiol Dis.* 2024;192:106432. doi:10.1016/j.nbd.2024.106432
12. Wan Y, Shen J, Ouyang J, et al. Bibliometric and visual analysis of neutrophil extracellular traps from 2004 to 2022. *Front Immunol.* 2022;13:1025861. doi:10.3389/fimmu.2022.1025861. Erratum in: Front Immunol. 2022;13:1098082. doi: 10.3389/fimmu.2022.1098082.
13. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372: n71. doi:10.1136/bmj.n71
14. Langfelder P, Horvath S. WGCNA: an R package for weighted correlation network analysis. *BMC Bioinf.* 2008;9(1):559. doi:10.1186/1471-2105-9-559
15. Aria M, Cuccurullo C. Bibliometrix: an R-tool for comprehensive science mapping analysis. *J Informetrics.* 2017;11(4):959–975. doi:10.1016/j.joi.2017.08.007
16. Jiang ST, Liu YG, Zhang L, et al. Immune-related adverse events: a bibliometric analysis. *Front Immunol.* 2022;13:1096806. doi:10.3389/fimmu.2022.1096806
17. Franceschi C, Abbracchio MP, Barbieri D, et al. Purines and cell death. *Drug Dev Res.* 1996;39(3–4):442–449. doi:10.1002/(SICI)1098-2299(199611/12)39:3/4<442::AID-DDR26>3.0.CO;2-1
18. Pelegrin P, Surprenant A. Pannexin-1 mediates large pore formation and interleukin-1beta release by the ATP-gated P2X7 receptor. *EMBO J.* 2006;25(21):5071–5082. doi:10.1038/sj.emboj.7601378
19. Feng J, Mu XM, Wang W, et al. A topic analysis method based on a three-dimensional strategic diagram. *J Inf Sci.* 2021;47(6):770–782. doi:10.1177/0165551520930907
20. Mohammadi E, Karami A. Exploring research trends in big data across disciplines: a text mining analysis. *J Inf Sci.* 2022;48(1):44–56. doi:10.1177/0165551520932855
21. Sluyter R. The P2X7 Receptor. *Adv Exp Med Biol.* 2017;1051:17–53. doi:10.1007/5584_2017_59
22. Tang NFR, Heryanto H, Armynah B, et al. Bibliometric analysis of the use of calcium alginate for wound dressing applications: a review. *Int J Biol Macromol.* 2023;228:138–152. doi:10.1016/j.ijbiomac.2022.12.140
23. Reed DA, Cook DA, Beckman TJ, et al. Association Between Funding and Quality of Published Medical Education Research. *JAMA.* 2007;298 (9):1002–1009. doi:10.1001/jama.298.9.1002
24. Wang YJ, Li ZX, Gu HQ, et al. China Stroke Statistics: an update on the 2019 report from the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations. *Stroke Vasc Neurol.* 2022;7(5):415–450. doi:10.1136/svn-2021-001374
25. Li JY, Hu XD, Lan YB, et al. Global Trends in Agricultural Drone Research: institutions and Authorship Networks. *Trans Chin Soc Agric Eng.* 2021;37(09):328–339.
26. Springer. Purinergic Signalling. Available from https://link.springer.com/journal/11302. Accessed July 11, 2023.
27. Engel T. The P2X7 Receptor as a Mechanistic Biomarker for Epilepsy. *Int J Mol Sci.* 2023;24(6):5410. doi:10.3390/ijms24065410
28. Zhu X, Li Q, Song W, et al. P2X7 receptor: a critical regulator and potential target for breast cancer. *J Mol Med.* 2021;99(3):349–358. doi:10.1007/s00109-021-02041-x
29. Arnaud-Sampaio VF, Rabelo, Rabelo ILA, et al. The P2X7 Receptor in the Maintenance of Cancer Stem Cells, Chemoresistance and Metastasis. *Stem Cell Rev Rep.* 2020;16(2):288–300. doi:10.1007/s12015-019-09936-w

30. Pelegrin P, Surprenant A. The P2X(7) receptor-pannexin connection to dye uptake and IL-1beta release. *Purinergic Sig*. 2009;5(2):129–137. doi:10.1007/s11302-009-9141-7

31. Anderson CM, Nedergaard M. Emerging challenges of assigning P2X7 receptor function and immunoreactivity in neurons. *Trends Neurosci*. 2006;29(5):257–262. doi:10.1016/j.tins.2006.03.003

32. Yiangou Y, Facer P, Durrenberger P, et al. COX-2, CB2 and P2X7-immunoreactivities are increased in activated microglial cells/macrophages of multiple sclerosis and amyotrophic lateral sclerosis spinal cord. *BMC Neurol*. 2006;6(1):12. doi:10.1186/1471-2377-6-12

33. Zalpoor H, Akbari A, Samei A, et al. The roles of Eph receptors, neuropilin-1, P2X7, and CD147 in COVID-19-associated neurodegenerative diseases: inflammasome and JaK inhibitors as potential promising therapies. *Cell Mol Biol Lett*. 2022;27(1):10. doi:10.1186/s11658-022-00311-1

34. Zalpoor H, Akbari A, Nabi-Afjadi M, et al. Hypoxia-inducible factor 1 alpha (HIF-1α) stimulated and P2X7 receptor activated by COVID-19, as a potential therapeutic target and risk factor for epilepsy. *Hum Cell*. 2022;35(5):1338–1345. doi:10.1007/s13577-022-00747-9

35. Soy M, Keser G, Atagündüz P, et al. Cytokine storm in COVID-19: pathogenesis and overview of anti-inflammatory agents used in treatment. *Clin Rheumatol*. 2020;39(7):2085–2094. doi:10.1007/s10067-020-05190-5

36. Batista Simões JL, Sobierai LD, Pereira SM, et al. Therapeutic Potential of P2X7 Purinergic Receptor Modulation in the Main Organs Affected by the COVID-19 Cytokine Storm. *Curr Pharm Des*. 2022;28(22):1798–1814. doi:10.2174/1381612828666220713115906

37. Hu SQ, Hu JL, Zou FL, et al. P2X7 receptor in inflammation and pain. *Brain Res Bull*. 2022;187:199–209. doi:10.1016/j.brainresbull.2022.07.006

38. Di Virgilio F, Dal Ben D, Sarti AC, et al. The P2X7 Receptor in Infection and Inflammation. *Immunity*. 2017;47(1):15–31. doi:10.1016/j.immuni.2017.06.020