

A Bibliometric Analysis Using VOSviewer of Publications on The TRPM2 Channel

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ABSTRACT

The transient receptor potential melastatin 2 (TRPM2) is a Ca²⁺ permeable cation channel that is a cellular redox sensor. It has been determined that the TRPM2 channel plays an important role in various neurological disorders such as Alzheimer's and Parkinson's. So far, however, theme trends and knowledge structures for TRPM2 have yet to be studied bibliometrically. This research mainly aims to compare the scientific production of TRPM2 in the research area between countries and to evaluate the publication trend between 1997 and 2022. All publications are from the Web of Science Core Collection database from 1997 to 2022. Journals, countries, regions, institutions, authors, and research points were included. A total of 824 publications related to TRPM2 were reviewed in this report. The Journal of Biological Chemistry ranked top for publishing 31 articles. The United States had the highest number of publications (203). Nazıroğlu M. from Süleyman Demirel University was the most prolific author with 91 publications among the authors who have TRPM2-related publications worldwide during the indicated period. Our study also combined bibliometric work with a systematic review of TRPM2, highlighting the four research limits of TRPM2. This is the first study to show trends and future developments in TRPM2 publications and to provide a clear and intuitive profile for contributions in this field.

Keywords: Bibliometric, TRP channels, TRPM2, Web of Science, VOSviewer

Introduction

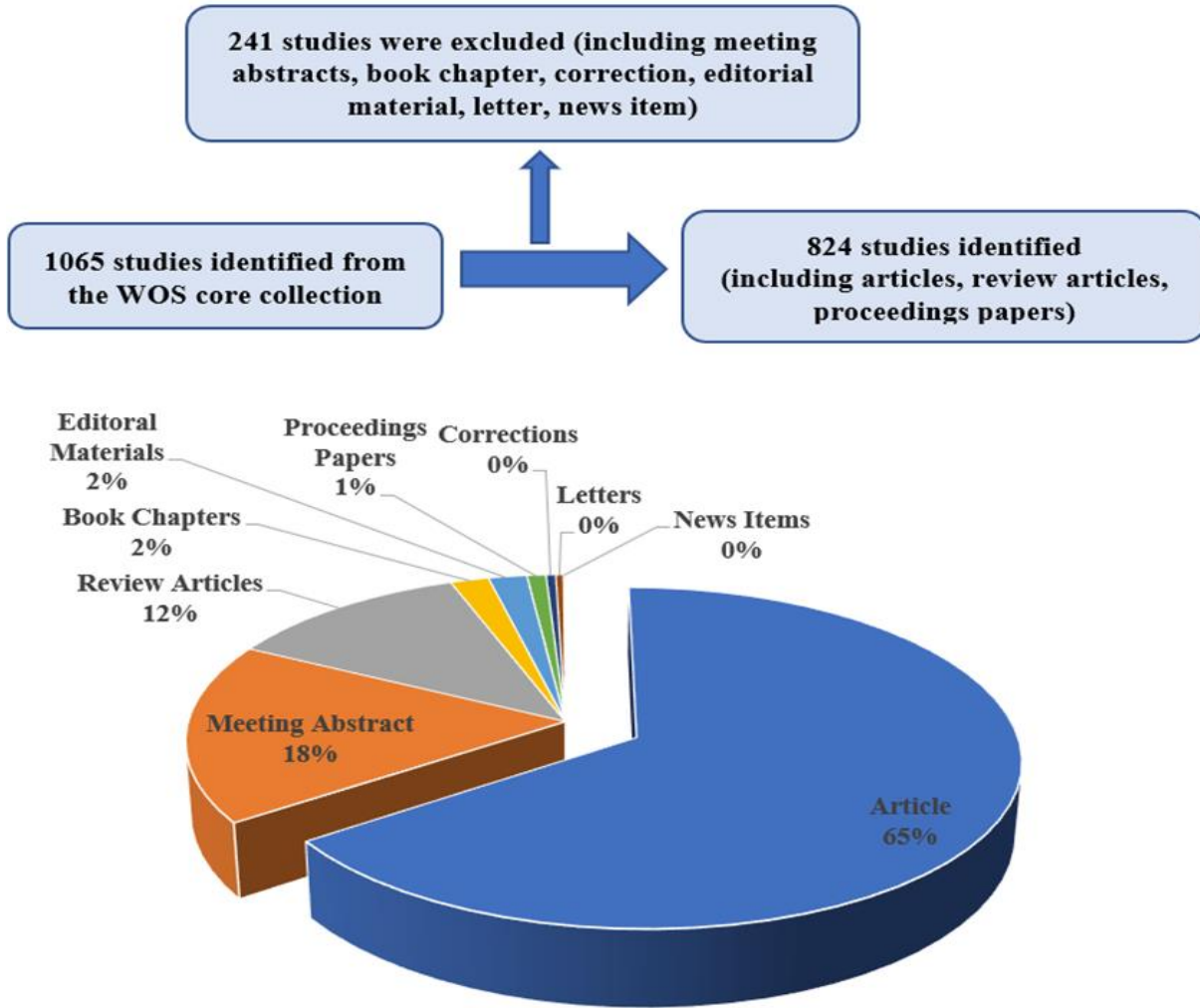
Transient Receptor Potential (TRP) cation channels were detected for the first time in photoreceptor cells of *Drosophila melanogaster* (1). TRP channel superfamily in mammals was divided into six subfamilies with 28 subtypes based on their specific binding sites (2). TRPV (vanilloid), TRPM (melastatin), TRPC (canonical), TRPA (ankyrin), TRPML (mucolipin), and TRPP (polycystin) are all members of the TRP family (3). According to their permeability to Ca²⁺ and Mg²⁺ ions, eight members of the TRPM family are categorized into four categories (TRPM1-3, TRPM2-8, TRPM4-5, TRPM6-7). TRPM2, TRPM6, and TRPM7 channels have enzymatic domains in their C-terminal region. While TRPM4-5 channels are not permeable to Ca²⁺ ions, TRPM6-7 shows high permeability to Ca²⁺ and Mg²⁺ ions (4,5). The TRPM2 channel was first identified in cancer (melastatin) cells in 1998. TRPM2 channels have been detected in many tissues and cells (6). TRPM2 has intracellular N-terminal and C-terminal ends and its transmembrane domain. It has been reported that the enzymatic region (NUDT9-H) located on the

C terminal is the specific binding site for adenosine diphosphate ribose (ADPR), which is representative of oxidative damage in the cell (7). Studies indicate that TRPM2 is a potential target for various central nervous system (CNS) diseases, including brain tumors. It further demonstrates that TRPM2 has multiple functions in cancer cells, ranging from maintaining viability to increasing sensitivities to chemotherapies or inducing cell cycle arrest and apoptosis, all representing potential targets for new therapeutic approaches (8). For these reasons, TRPM2 draws the interest of scientists, and the number of research on TRPM2 is growing.

Bibliometric analysis is a useful method that helps researchers to analyze and explore large amounts of scientific data. This method allows us to understand how a particular field of study is changing over time and to identify new areas of research that are becoming more important. It's a tool that helps us better understand scientific research history and future direction. Bibliometric studies are the numerical analysis of the publications produced by individuals or institutions in a certain area, in a certain period

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Graphical abstract: The flowchart and percentage of the type retrieved document of TRPM2 research

and region, and the relations between these publications (9).

Our literature review has not found bibliometric studies showing trends in TRPM2 research activity. With this feature, the first bibliometric research on TRPM2 was conducted for the first time with this study. In this research, we aimed to present a report on scientific production among countries in the field of TRPM2 in the last 25 years (1997 – 2022) and to review relevant trends and clusters.

Material and methods

Design of the Study: This observational, descriptive, and retrospective study utilized the scientometric technique and scientific mapping. It complied with the Helsinki Declaration, which was revised in 2013. Ethics committee approval is not required as no human or animal research exists.

To discover TRPM2 research documents, the literature studies were obtained online via the Web of Science (WoS) bibliographic database on June 14, 2022 (Clarivate Analytics, Philadelphia, USA). We collected 25 years of data from 1997 to 2022 to identify the publication trend. All literature access and record downloads were completed on June 14, 2022, to avoid changes in citation numbers due to daily database updates. The journals, the authors and affiliations (institution or organization and country), the years that the articles were published, the citation numbers, the scientific categories, the keywords, and automatically generated from the titles of the articles were all obtained using WoS. The descriptive analysis of the publication years, citation counts, scientific categories, first authors, affiliations, nations, and journals were carried out using Microsoft Excel.

Data Collection: On June 14, 2022, a comprehensive search was conducted in the WoS of the ISI Web of Science (Thomson Reuters,

Philadelphia, PA, USA) online database. This database contains articles from high-impact, highest scientific journals worldwide.

Terms and retrieval techniques used were as follows: The MESH keywords (TRPM2*) were used. The title (TI) field and only the Science Citation Index Expanded (SCI-EXPANDED) index was used for the search queries.

The following inclusion and exclusion criteria were applied:

The search keywords entered in the database are TRPM2,

1- The studies published after the end of June 14, 2022, were excluded;

2- Only the SCI-EXPANDED index was used for the search queries.

3- Language: English

4- Document Types: Article, Review Article, and Proceedings Paper (total of the 824 studies identified).

Mapping: VOSviewer version 1.6.18 (Leiden University, Leiden, The Netherlands) was used to analyze. This study partially modified Zhang et al. and Yu et al. from their studies (9,10). In the figures, Cooperation is depicted by lines connecting nations. Thicker lines indicate stronger cooperation. Countries with larger perimeters or text sizes had higher levels of international cooperation. A scale automatically placed below the figure in the VOSviewer program has been added to demonstrate this.

Statistical Analysis: We evaluated the online “WoS Literature Analysis Report” output data and features, including distribution of countries/regions, institutions, journals, and authors, the annual number of publications, and citations. Regarding the TRPM2 channel, the Author with the most articles, citations of organizations/universities, citations of countries, and most used keywords, and author/citation collations were calculated via VOSviewer version 1.6.18

Results

General information: A total of 1065 TRPM2-related studies were identified from the WoS core collection, and approximately 241 studies were excluded (including meeting abstracts, book chapters, corrections, and editorial material, letters, and news items). A total of 824 studies were scanned, including the remaining 714 articles

(65%), 100 reviews (12%), and 10 proceedings papers (1%). The search criteria produced 824 pieces of literature, and the flowchart of the literature containing these terms is shown in the Graphical abstract.

Number of publications and citations, outstanding country and influential authors:

The chronological distribution of the number of broadcasts on the TRPM2 channel between 1997 and 2022 is shown in Figure 1A. Although the number of publications was low initially, it was observed to have gained rapid momentum in 2006. It has increased steadily over the years with some fluctuations. The highest number of publications was in 2020 (84), and Figure 1A shows that the topic of TRPM2 has recently gained attention among scientists. Considering the number of citations by year, it is observed that there has been an increase in the number of citations in parallel with the number of publications in the last 25 years. It shows the most cited time with 713 citations in 2011. Over 600 citations have been produced concerning the TRPM2 channel over the last decade (Figure 1B). The outstanding countries with the highest number of publications among the specified dates are the USA (203), China (153), Turkey (127), Japan (119), Germany (103) and England (93). Related to TRPM2, the top six on the list of top-publishing authors are Naziroğlu M., Mori Y., Jiang LH., Yang W., Luchoff A., and Miller BA. (Figures 1C and D).

The co-authoring visualization analysis of authors with VOSviewer: A total of 3521 researchers participated in the publication of the received documents. Figure 2 shows co-authoring visualization analysis by authors using the VOSviewer technique of minimum 4 document productivity. The map contained 147 circles, each representing an author. The top six authors with more publications have a larger circle than the others. Closed circles indicate authors with close research collaborations. The most influential authors in this field mentioned in Figures 1C and D and other researchers collaborating with them are associated in Figure 2.

The most effective institutions for visualization analysis with VOSviewer: The citations of organizations were analyzed, as shown in Figure 3. Süleyman Demirel University in Turkey has the highest number of publications,

Table 1. The top 10 Institutions Contributed to The Publications on TRPM2 Research

Rank	Institution	Country	Frequency (n=824)	Percentage (%)
1	Süleyman Demirel University	Turkey	93	11.232
2	Kyoto University	Japan	56	6.763
3	University of Leeds	UK	52	6.280
4	Zhejiang University	China	38	4.589
5	League of European Research Universities (LERU)	Belgium	32	3.865
6	University of Hamburg	Germany	27	3.261
7	Rwth Aachen University	Germany	26	3.140
8	Xinxiang Medical University	China	25	3.019
9	National Institutes of Natural Sciences in Japan	Japan	22	2.657
10	Pennsylvania Commonwealth System of Higher Education Pcshe	China	22	2.657

Table 2. The top 10 Journals That Published Articles on TRPM2 Research

Rank	Journal Title	Frequency (n=824)	Percentage (%)	IF 2021
1	Journal of Biological Chemistry	31	3.744	5.157
2	Scientific Reports	30	3.623	4.380
3	Cell Calcium	20	2.415	6.817
4	Molecular Neurobiology	17	2.053	5.560
5	British Journal of Pharmacology	14	1.691	8.31
6	International Journal of Molecular Sciences	14	1.691	6.01
7	Journal of Membrane Biology	13	1.570	2.19
8	Pflugers Archiv European Journal of Physiology	13	1.570	3.657
9	Plos One	12	1.449	3.58
10	Journal of Physiology London	10	1.208	5.182

with a rate of 11.232 (n=93). The second-best institution is Kyoto University in Japan, with a rate of 6,763% (n=56). Other top institutions are China, Belgium, Germany, and Japan universities. In addition, the collaborations of institutions with each other were visually presented with VOSviewer analysis (Table 1).

The citations of countries for visualization analysis with VOSviewer: The threshold (32 appears) is in 35 countries. The countries with the highest number of citations are the USA, Turkey, Japan, Germany, and England, and the citation relationship between countries was visualized through the VOSviewer program (Figure 4).

Analysis within author keywords and network map of authors in publications on TRPM2 channel research: It shows 80 of the keywords of 798 authors who have been mentioned at least 3 times in the publications related to the TRPM2 channel. The keywords have been organized into

four distinct groups. Other keywords such as TRPM2, TRPM2 channel, oxidative stress, calcium, and ADP-ribose were widely used (Figure 5). The network map of authors that conducted TRPM2 research. The citations of authors with a minimum number of four documents per author. The threshold was set at 1726 authors (78 clusters appear in Figure 6).

The journals that published articles and top 10 publications on TRPM2 channel research:

Table 2 lists the top ten journals by several publications in TRPM2 channel searches. Journal of Biological Chemistry ranked first with 31 or 3.7%, followed by Scientific Reports with 30 (3.6%), Cell Calcium with 20 (2.4%) documents, Molecular Neurobiology with 17 (2.0%), British Journal of Pharmacology with 14 (1.6%), International Journal of Molecular Sciences 14 (1.6%), Journal of Membrane Biology with 13 (1.5%), Pflugers Archiv European Journal of

Table 3. The top 10 Publications on TRPM2 Research

Rank	Title	Number of citations	Reference
1	TRPM2-mediated Ca ²⁺ influx induces chemokine production in monocytes that aggravates inflammatory neutrophil infiltration	414	(11)
2	TRPM2 activation by cyclic ADP-ribose at body temperature is involved in insulin secretion	289	(12)
3	Accumulation of free ADP-ribose from mitochondria mediates oxidative stress-induced gating of TRPM2 cation channels	252	(13)
4	Cyclic ADP-ribose and hydrogen peroxide synergize with ADP-ribose in the activation of TRPM2 channels	241	(14)
5	New molecular mechanisms on the activation of TRPM2 channels by oxidative stress and ADP-ribose	239	(15)
6	TRPM2 channel opening in response to oxidative stress is dependent on activation of poly (ADP-ribose) polymerase	221	(16)
7	Critical intracellular Ca ²⁺ dependence of transient receptor potential melastatin 2 (TRPM2) cation channel activation	210	(17)
8	TRPM2 links oxidative stress to NLRP3 inflammasome activation	207	(18)
9	TRPM2 Functions as a Lysosomal Ca ²⁺ -Release Channel in beta Cells	203	(19)
10	Hydrogen peroxide and ADP-ribose induce TRPM2-mediated calcium influx and cation currents in microglia	199	(20)

Physiology 13 (1.5%), Plos One Journal of Physiology London with 12 (1.4%) and 10 (1.2%) documents (Table 2). The 10 most popular articles related to the TRPM2 channel are listed in Table 3.

Discussion

Scientists conduct bibliometric analysis for various reasons, including identifying emerging trends in article and journal performance, collaboration trends, and study topics, as well as investigating or researching the intellectual makeup of a particular field in previous studies. Bibliometric analysis has gained immense popularity in medical research over the past few years (9,10,21). In conclusion, a well-executed bibliometric study puts a topic in front of the researcher in unique and meaningful ways, allowing the researcher to see the overall picture. Our literature review found no bibliometric study about the TRPM2 channel. This study is important because of the increasing number of studies on the TRPM2 channel and the fact that the channel appears to play a role in the ethology of many diseases. TRPM2 is generally expressed in the brain (22), heart (23), lung, liver,

skeletal muscle, leukocytes and pancreas (24,25). At cellular levels, neurons (26-28), microglia (29), astrocytes (30), macrophages (31), neutrophils (32), dendritic cells (33), megakaryocytes (34), vascular endothelial cells (35) were reported to be expressed. TRPM2 channel has been associated with various neurological disorders, including Alzheimer's disease, neuropathic pain, Parkinson's disease, migraine, ischemia/stroke, and bipolar disorder, and it has been argued that it may play an important role in treating these diseases (36,37).

Our bibliometric study of TRPM2 shows some key publication patterns between 1997 and 2022. A total of 1065 TRPM2-related studies were identified from the WoS core collection, and a total of 824 studies were scanned (articles, reviews, and proceedings), accounting for 78% of the total studies. Between 1997 and 2004, there was a limited number of publications (fewer than 10 documents), whereas the number of publications from 2005 had some fluctuations and was the highest in 2020 (Figure 1A). This finding was consistent with other bibliometric studies of TRP channels (9,38). It was determined that the highest number of participants in TRPM2 research

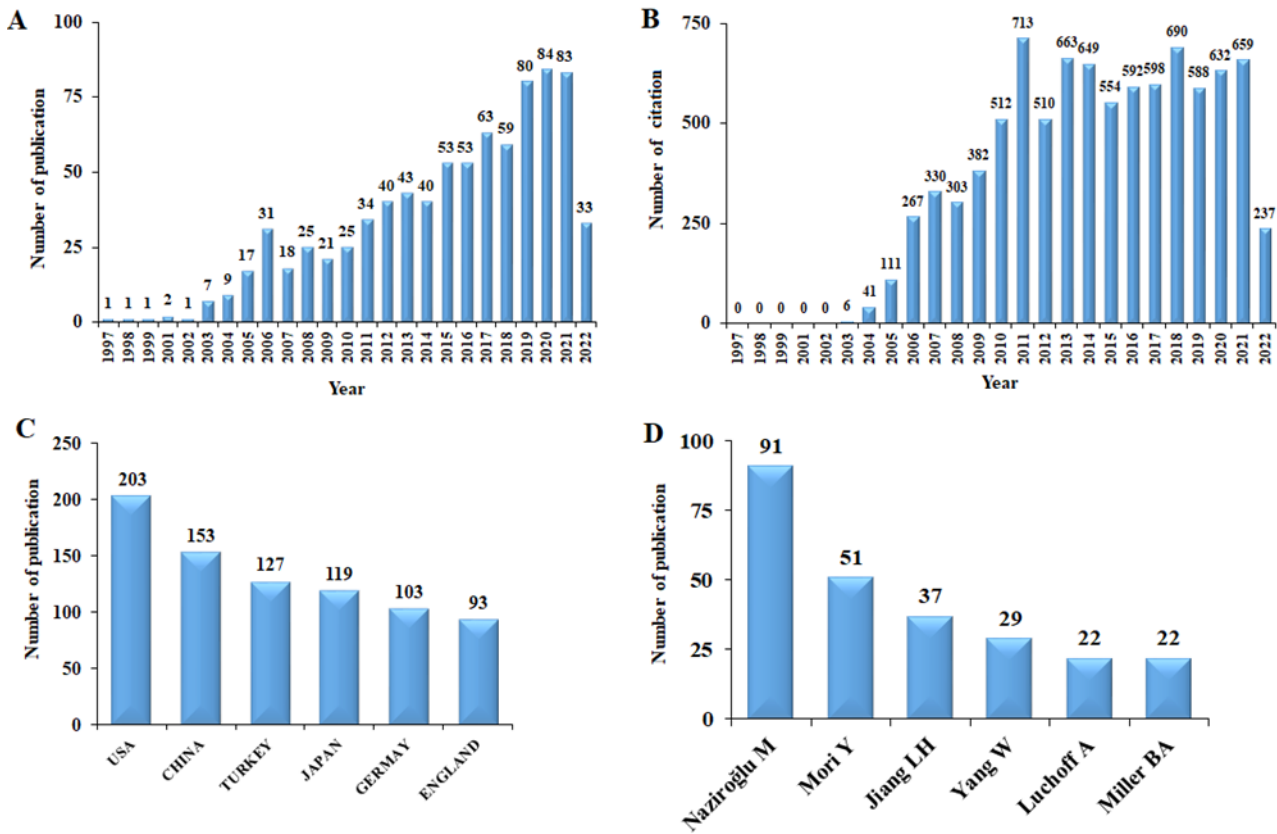


Fig.1. The number of publications by year (A), the number of cited times by year (B), in the top 6 countries (C), and the top 6 authors by the number of publications (D)

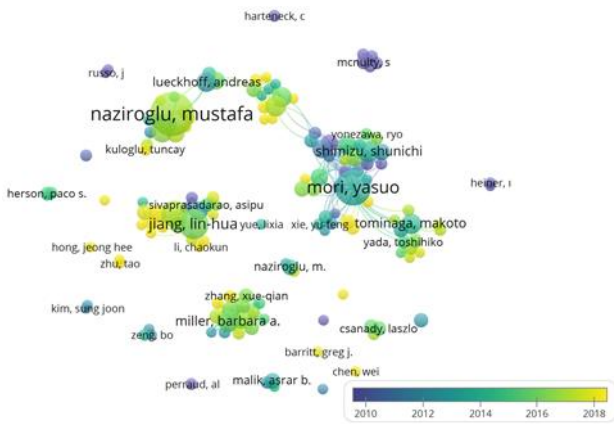


Fig. 2. Co-authorship authors with 4 minimum numbers of documents to an author. The 3521 authors reach the threshold (147 appear in the figure). Different colours indicate different clusters, and the size of the circles indicates the number of articles

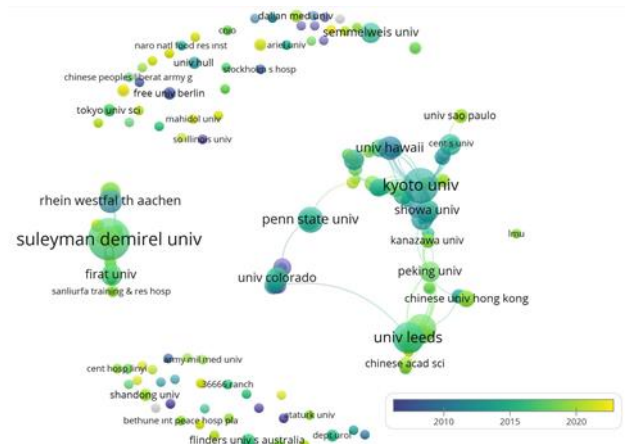


Fig. 3. The citations of organizations. The 441 organizations are the threshold (441 appears in the figure). Süleyman Demirel University in the green cluster is the most cited organization (60 times). Different colours indicate different clusters, and the size of the circles shows the counts of the citations of organizations

was in 2011 (Figure 1B). The United States contributed the most to TRPM2 research, while China, Turkey, and Japan have significantly contributed to the development of this discipline (Figure 1C). Figure 1D also displays the authors with the most publications on TRPM2. In addition, we have shown the author’s production was explained, it was determined that

reactive oxygen species-induced chemokines were Contributions (Figure 2), the institutions that work the most in this field (Figure 3 and Table 1), the countries where the most cited publications are published (Figure 4), and the keywords in the

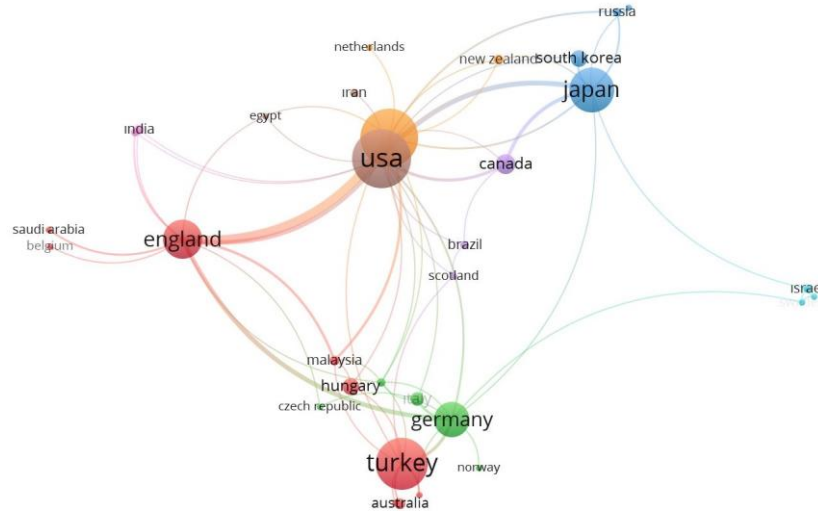


Fig. 4. The citations of countries. In the 35 countries, the threshold (32 appears in the figure). Different colors indicate different clusters, and the size of the circles shows the counts of the citations of countries

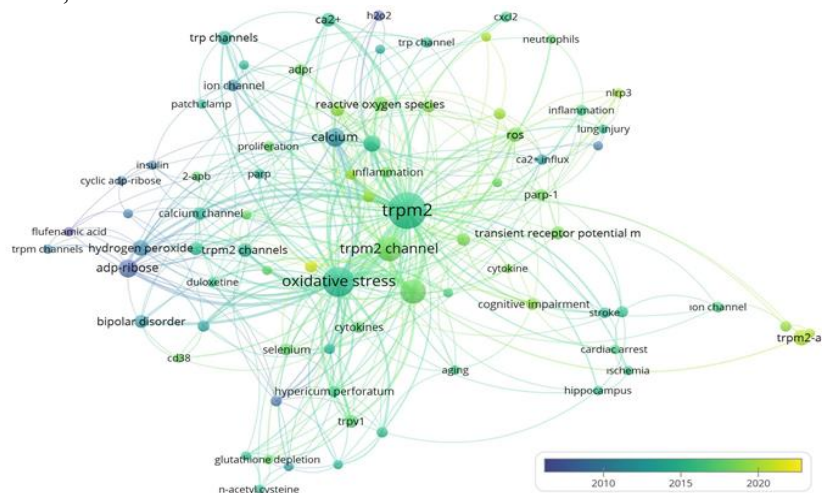


Fig. 5. Keywords map showing the network visualization (top) and overlay visualization (bottom) of 798 keywords that occurred at least 3 times in publications on TRPM2. Different colours indicate different clusters, and the size of circles indicates the counts of the keywords

studies about the TRPM2 channel (Figure 5) and the citation network for this study (Figure 6).

"TRPM2-mediated Ca^{2+} influx stimulates chemokine synthesis in monocytes that aggravate inflammatory neutrophil infiltration" (11), which was published in Nature Medicine, was the most referenced paper from research on the TRPM2 channel (Table 3). In this study, in which the functional role of TRPM2 in chemokine It has been shown that TRPM2 controls ROS-induced chemokine production in monocytes by allowing Ca^{2+} entry into human U937 monocyte cells. The second most cited article, "TRPM2 activation by cyclic ADP-ribose at body temperature is involved in insulin secretion" (12), was published in The EMBO Journal in 2006. This original article determined that TRPM2 activation by cyclic ADP-ribose at body temperature plays a role in insulin secretion. The third most cited article,

"Accumulation of free ADP-ribose from mitochondria mediates oxidative stress-induced gating of TRPM2 cation channels" (13), was also published in The Journal of Biological Chemistry in 2005.

This study used WOS data and bibliometric analysis to examine the characteristics of TRPM2 channels research results from 1997 to 2022. The number of broadcasts on TRPM2 channels remained above 824 yearly (after the specified eliminations were made). Based on current global trends, the number of publications on TRPM2 research shows that it will increase dramatically. This study argued that the accumulation of free ADP-ribose, mitochondrial or other oxidative stress sources might trigger metabolic disorders associated with a disease or ageing through the TRPM2 channel. Bibliometric analysis of the literature on the TRPM2 channel helps researchers

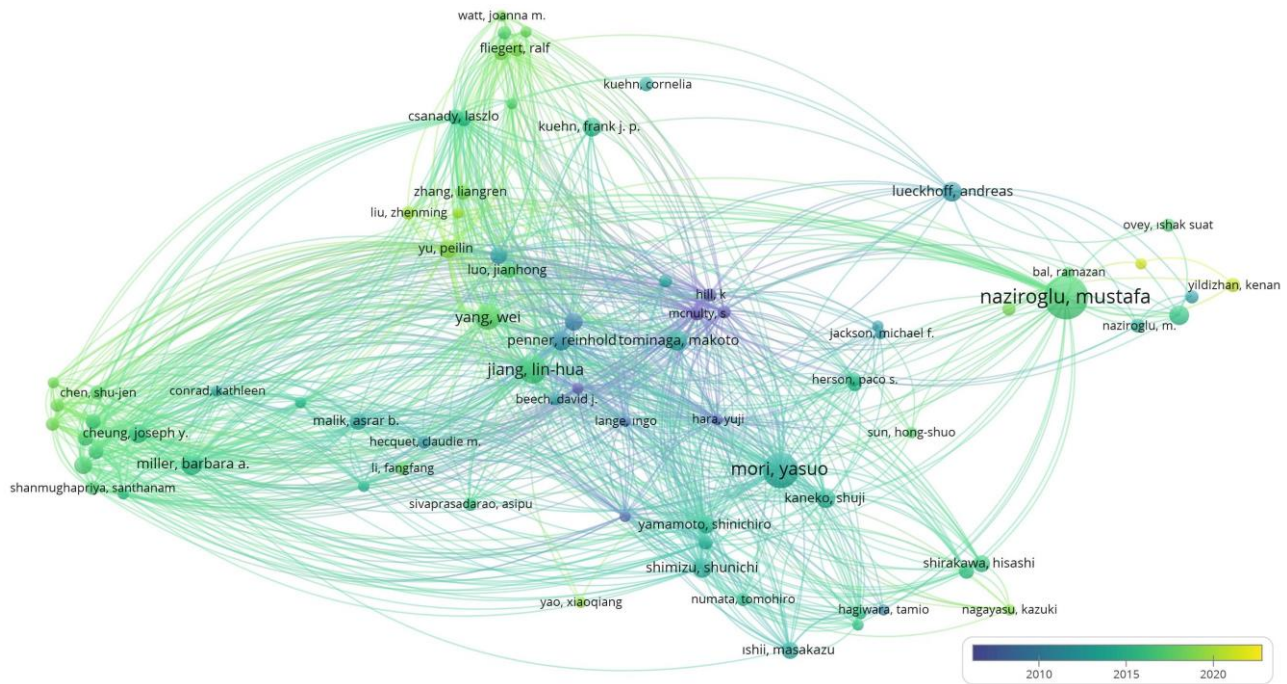


Fig. 6. The network map of authors that conducted TRPM2 research. The citations of authors with 4 minimum number of documents to an author. The 1726 authors the threshold (78 appears in the figure). Different colors indicate clusters, and the circle size indicates the authors' network map counts responsible for recruiting inflammatory cells to the sites of injury or infection

identify collaborations and find research hotspots. It will contribute to estimating the limits of the Ca^{2+} channel research.

Strengths and Limitations: This is the first bibliometric analysis to focus on TRPM2 trends. The data downloaded from WoS covered the vast majority of articles in the field of TRPM2 research, and the data analysis was relatively objective and comprehensive, clearly showing the status of TRPM2. However, this study only consists of original articles and reviews published from 1997 to 2022. It had a few limitations, such as the inability to review and analyze articles from publications not indexed in the WoS indexes. Also, articles in other languages were excluded, as the language of the article and keywords were only in English. Only the types of articles, review articles and proceedings were included in the study. Other databases (such as Scopus) were excluded from the study.

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