Review Article

Navigating TRPML1 Scholarly Hotspots Through a Bibliometric Lens

Lutfia Ilsahaida Abdul Malik[1], Aisyah Hasyila Jahidin[1]* and Mizaton Hazizul Hasan[1]

[1]Department of Pharmacology & Life Sciences, Faculty of Pharmacy, Universiti Teknologi MARA Cawangan Selangor, Puncak Alam Campus, 42300, Selangor, Malaysia

ABSTRACT

Transient Receptor Potential Mucolipin 1 (TRPML1) is a calcium-permeable cation channel predominantly localised on late endosomes and lysosomes. Its multifaceted roles encompass lysosomal exocytosis, autophagy, and cellular processes, such as mitochondrial function and cancer cell invasion. Despite extensive research on TRPML1, there remains a need to systematically evaluate TRPML1-related studies for the scientific community. Our goals were to analyse TRPML1 research publications to pinpoint key contributors, trends, and major themes. The aim is to showcase significant discoveries and untapped areas within TRPML1 for future research endeavours. In this study, we employed bibliometric tools, specifically VOSviewer, to quantitatively analyse TRPML1 publications. TRPML1 research witnessed an upward trajectory, peaking in 2019. The United States emerged as the predominant contributor, with China gaining prominence in recent years. The Journal of Biological Chemistry stood out as a leading disseminator of TRPML1-related findings. Additionally, Nature and Nature Communications boasted the highest citation rates, emphasising the impact of TRPML1 research. Highly cited articles unravelled TRPML1's pivotal role in iron homeostasis and autophagy regulation, shaping scholarly discourse and therapeutic advancements. Author networks spotlighted influential contributors such as Haoxing Xu, and Susan A Slaugenhaupt. Keyword analysis identified clusters related to lysosomal disorders, cellular regulations, and cellular stress, providing insights into prevailing research priorities. Initially, TRPML1 research centered on understanding its role in endosomes and lysosomes, revealing its relevance in various physiological and pathological conditions. However, certain underexplored research avenues for TRPML1 deserve attention, particularly in the context of autophagy and cancer. Finally, this study explored seven key research frontiers of TRPML1, illuminating critical areas namely podocyte function, exosome release, neurodegeneration, autophagy regulation, cancer progression, apoptosis, and interactions with reactive oxygen species. By delving deeper into these domains, researchers can enhance their understanding of TRPML1 and potentially open avenues for innovative disease interventions.

Keywords: TRPML1, mcoln1, VOSviewer, bibliometric analysis, calcium signalling

Corresponding author:
Aisyah Hasyila Jahidin
Faculty of Pharmacy, Universiti Teknologi MARA (UiTM) Selangor Branch
Puncak Alam Campus, 42300, Selangor, Malaysia
Email: aisya735@uitm.edu.my

Received: 15 Mar 2024; accepted: 25 June 2024
Available online: 30 June 2024
http://doi.org/10.24191/IJPNaCS.v7i1.07

1.0 Introduction

Transient Receptor Potential Mucolipin 1 (TRPML1) is a calcium (Ca^{2+}) channel predominantly localised on lysosomes. It emerges as a critical player in diverse cellular processes. Studies showcase TRPML1's involvement in regulating mitochondrial function in hepatocellular carcinoma cells (1), mediating lysosomal exocytosis, tissue repair, positioning, and autophagy (2), as well as facilitating zinc (Zn^{2+}) signals in neurons (3). TRPML1's impact extends to regulating mitochondrial Ca^{2+} dynamics (4), large particle phagocytosis (5), autophagosome biogenesis (6), and smooth muscle contractility in the lower urinary tract (7). Additionally, TRPML1 is implicated in autophagy, lysosome function, and disease pathogenesis (8), with its activation associated with promoting autophagic clearance and protecting motor neurons (9). Furthermore, TRPML1 modulates protein homeostasis in melanoma cells, emphasizing its multifaceted roles in cellular functions from autophagy and lysosomal processes to mitochondrial dynamics and disease pathogenesis (10).

Bibliometric analysis is a sophisticated and quantitative methodology which plays an indispensable role in scientific research. By systematically examining written publications, it uncovers core research areas, identifies influential authors, and reveals intricate scholarly relationships (11). This approach, facilitated by computer-assisted review techniques, provides insights into evolving research trends and scholarly networks, becoming a vital tool for objectively evaluating scientific production and productivity (12). In scientific research, bibliometric analysis extends to measuring research impact, transparently assessing productivity, and identifying key topics for future exploration (13). Its benefits extend to a diverse audience, including researchers, institutions, policymakers, and funding agencies, offering nuanced understandings of global research trends, collaborative efforts, and overall impact (14). Nevertheless, recognising its limitations, such as the risk of misuse and the complexities involved in interpreting intricate data visualisations, is crucial. This underscore for the importance of adopting a nuanced and prudent approach when applying it (15).

This paper presents a comprehensive bibliometric analysis of TRPML1 research, addressing a significant quantitative gap in the existing literature, which is abundant with narrative reviews but lacks such analysis. Our study aims to enhance the understanding of this topic by assessing the TRPML1 research landscape, uncovering publication trends, citation patterns, and author dynamics. We delve into key research frontiers such as podocyte function, exosome release, neurodegeneration, autophagy regulation, cancer progression, apoptosis, and interactions with reactive oxygen species (ROS). By examining journal distributions, highly cited works, and authorship trends, we aim to gauge the scholarly impact and recognition of TRPML1 research. This in-depth analysis offers valuable insights into the dynamics, significance, and future directions of TRPML1 research, spotlighting its critical areas and paving the way for future research avenues and therapeutic interventions for diseases associated with TRPML1 dysregulation.

2.0 Methods

2.1 Bibliometic Tools

In this study, Scopus was selected as the search database due to its comprehensive attributes. These include its extensive coverage, high-quality peer-reviewed content, detailed citation data, robust author and institutional metrics, advanced analytical tools, frequent updates, user-friendly interface, and interdisciplinary

reach. Redundant and irrelevant data were removed through a manual screening process. The refined data were then exported to software applications such as Microsoft Excel, Publish or Perish, and VOSviewer for in-depth analysis.

Microsoft Excel, known for its adaptability and support for multiple file formats like .csv (Comma Separated Values), was used for flexible data manipulation. Publish or Perish, which typically interacts with RIS (Research Information Systems) files, was utilized for bibliographic data. VOSviewer, capable of accepting various file formats such as .txt, .csv, and .bib (BibTeX), was used, with .txt or .csv formats being recommended for data import.

In the data analysis phase, Microsoft Excel was used for descriptive analyses, including publication frequency per year, journal distribution, countries, and list of authors. Citation metrics like total citations and cites/paper were analysed using Publish or Perish. VOSviewer was employed for co-occurrence analysis of keywords, co-authorship, and the creation of visual network maps.

Following data analysis, graphs and charts were generated using Microsoft Excel or VOSviewer to showcase publication trends and research collaborations. These visualizations were interpreted to extract meaningful insights, identifying trends, key contributors, and emerging research areas. The findings were compiled into a comprehensive report, with integrated visualizations to support the analysis. The report underwent thorough review and revision to ensure accuracy, clarity, and coherence, culminating in a high-quality final document.

2.2 Procedural Steps and Analysis

Data retrieval was conducted via the Scopus database on February 20, 2024 using the following search queries: (TITLE(trpml1 OR mcoln1 OR "mucolipin-1" OR "mucolipin trp cation channel 1" OR "transient receptor potential mucolipin 1" OR trpm-l1 OR trp-ml1) AND KEY (trpml1 OR mcoln1 OR "mucolipin-1" OR "mucolipin trp cation channel 1" OR "transient receptor potential mucolipin 1" OR trpm-l1 OR trp-ml1)) AND (LIMIT-TO(DOCTYPE, "ar") OR LIMIT-TO(DOCTYPE , "re")) AND (LIMIT-TO(LANGUAGE, "English")). This exercise was completed within one day to remove biases and any variances induced by potentially daily database upgrades.

The search terms were selected based on the extent of available literature on the topic and synonyms developed during discussions to address any potential conflicts. A team of three experts thoroughly reviewed and brainstormed the keywords associated with TRPML1, assessing each term individually to ensure the inclusion of all pertinent information.

The inclusion criteria for the analysis were specifically defined to encompass only original articles and reviews, with an additional requirement that these documents be written exclusively in English. Furthermore, with regard to the publication year, no restrictions were imposed, allowing for a comprehensive range of documents to be included in the study.

From the search, a total of 155 papers were obtained. The data, exported in CSV and RIS formats from the Scopus database, underwent a meticulous screening process by three experts. This process aimed to eliminate duplicates and identify any irrelevant entries. Upon examination, all data were found to be relevant, and thus, no exclusions were made from further analysis.

The data were then imported and analysed using Microsoft Excel 2019, Publish or Perish - Harzing.com, and the Java application VOS viewer 1.6.16. The process of analysis is illustrated in Fig. 1.

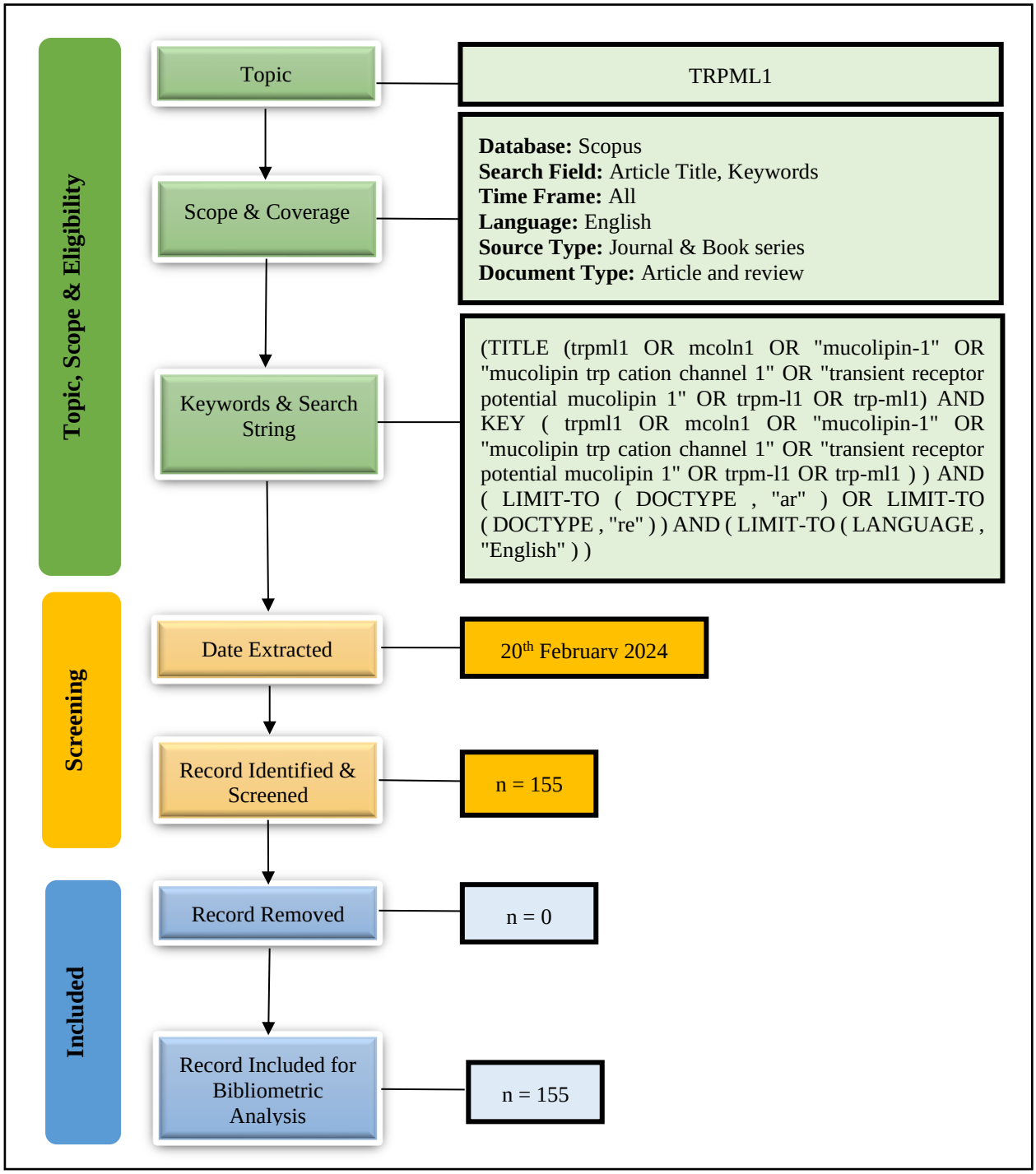


Figure 1: Flow Diagram of the search strategy and data exclusion

3.0 Results

3.1 Trends and type of publications

The Scopus database returned a total of 155 articles that fulfilled the search criteria. Fig. 2A illustrates the evolution of TRPML1 publications over the inaugural period. Despite fluctuations, the global output has exhibited an upward trend, peaking in 2019. Although the number of publications was low, citation counts were highest in 2006. In total, 94.84% of the published documents consisted of original articles (147 papers), while the remaining 5.16% were review papers (8 papers) (Fig. 2B).

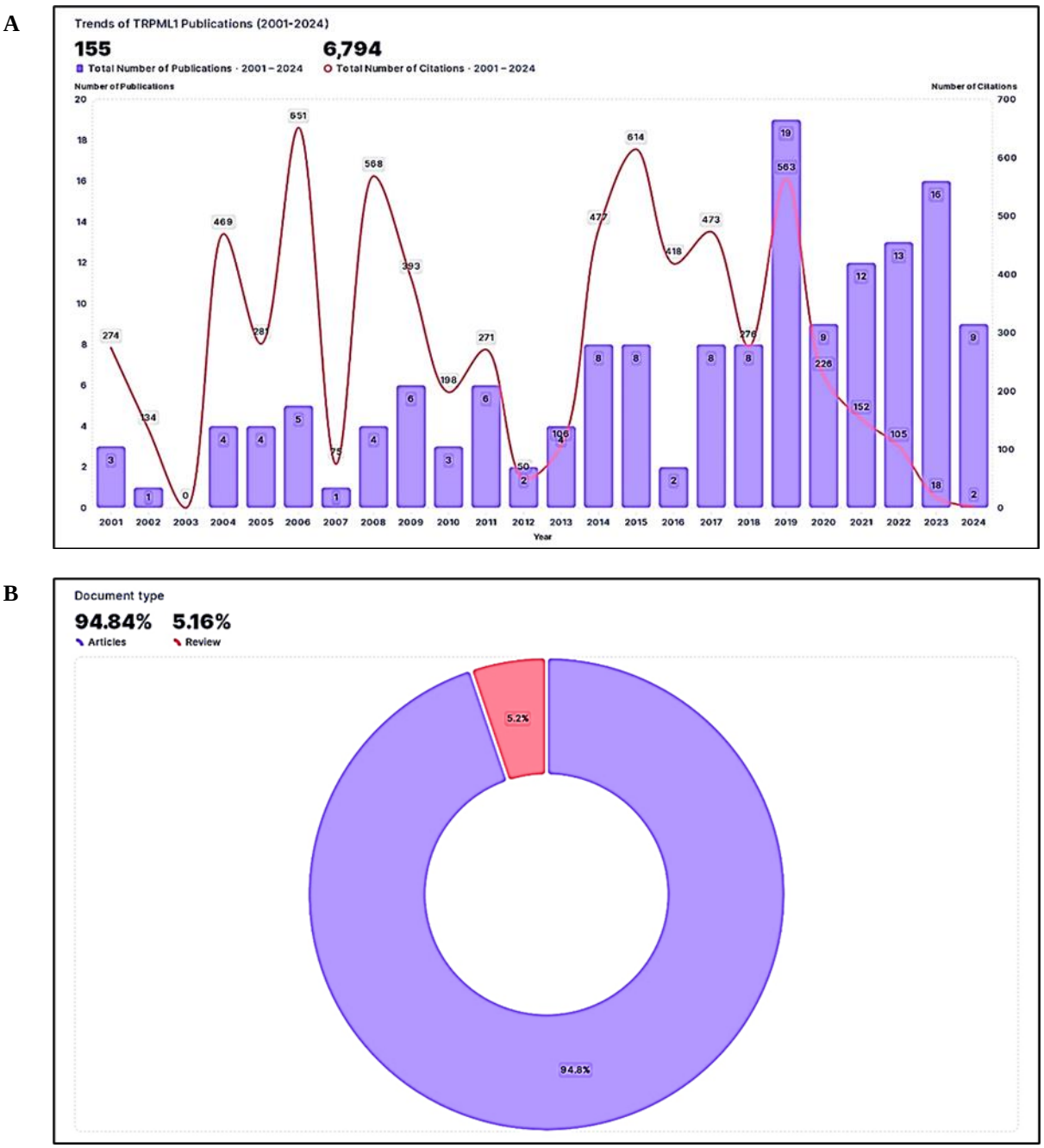


Figure 2: (A) Publications according to years. (B) Type of documents

3.2 Countries contributing to global publications and growing trends

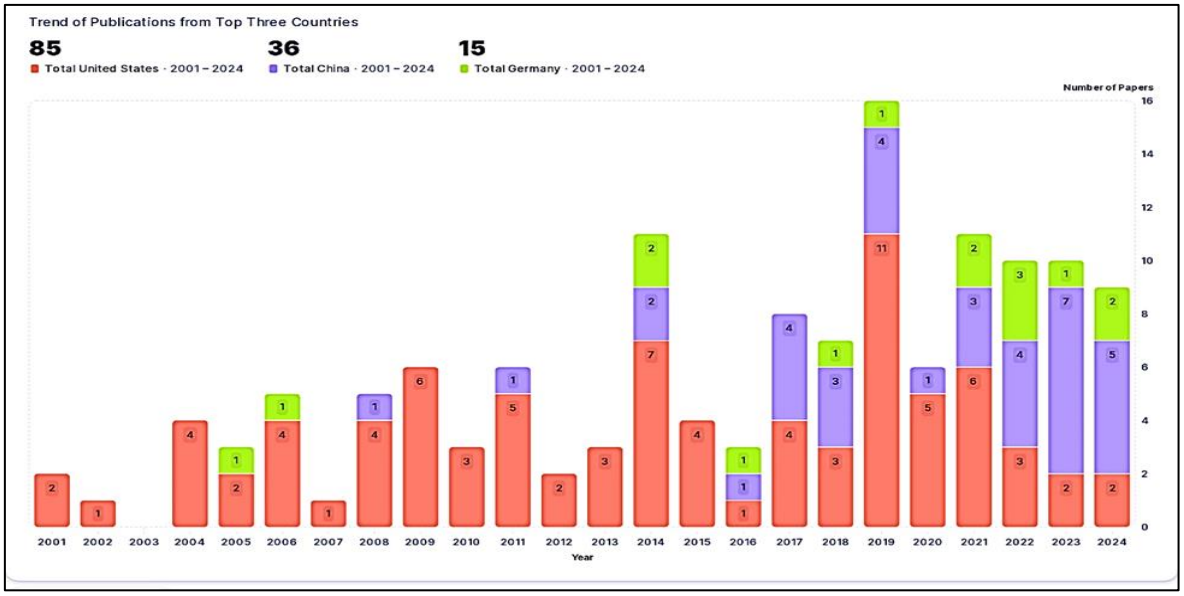
Twenty-six countries contributed to the publications on TRPML1 research (Appendix A). The top six countries were the United States (US) (85 publications, 54.83%), China (36 publications, 23.23%), Germany (15 publications, 9.68%), Canada (14 publications, 9.03%), the United Kingdom (UK) (12 publications, 7.74%), and Italy (11 publications, 7.10%). Other countries published less than 10 articles each. Collaborative efforts across borders were evident in some documents The significant co-authorship from the United States (11 links), Germany (7 links), and the United Kingdom (5 links) highlights the extensive international collaboration in research activities (Appendix B and C).

Fig. 3A highlights the top three countries based on the annual publication

count. Initially, the US was the sole contributor from 2001 until Germany joined in 2005, followed by China in 2008. However, China eventually surpassed the US in article production, dominating from 2022 onward. Remarkably, the US produced twice as many documents as China and Germany combined. Unsurprisingly, the US also received the highest number of citations (5, 500).

Interestingly, despite not ranking among the top three contributors in TRPML1 publications, both the UK and Canada received more citations than Germany. Noteworthy was Sweden's exceptional impact: with only one publication, it garnered a strikingly high maximum citation count of 429 (Fig 3B). This disparity underscored Sweden's unique influence in TRPML1 research.

A



B

Countries contributed to TRPML1 publications

Countries	Publications	Citations
United States	85	5.5k
China	36	1.3k
Germany	15	523
Canada	14	526
United Kingdom	12	540
Italy	11	301
Japan	7	113
Israel	5	178
South Korea	5	47
Australia	3	188
Argentina	2	167
Ireland	2	16
Switzerland	2	33
Austria	1	0
Brazil	1	1
Czech Republic	1	0
Denmark	1	0
France	1	83
Iraq	1	45
Netherlands	1	0
Oman	1	0
Pakistan	1	5
Spain	1	1
Sweden	1	429
Taiwan	1	10
Turkey	1	14

Figure 3: (A) Top three countries published the highest number of papers. (B) Countries with the total number of citations

3.3 Journal distribution and highly cited articles

The documents related to TRPML1 were primarily published in 87 different journals. Table 1 provides a list of the top 5 journals ranked based on number of paper/journal, along with statistical values such as Cites/paper or SJR (SCImago Journal Rank). SJR indicator assesses journal performance and article significance as of June 2023.

Among these top 5 journals, the Journal of Biological Chemistry stood out, publishing the highest number of TRPML1 articles (14 articles) with 68.86 cites per paper. Traffic followed in second place with 6 articles and 72.76 cites per paper. Autophagy, Cell Calcium, Nature Communication, and Proceedings of The National Academy of Sciences of The United States of America each tied for third place, each publishing 5 articles.

Nature boasted the highest SJR (18.51), with a rate of 212.00 cites for each paper. Following closely was Nature Communications (SJR 4.89, 127.80 cites/paper). On the other end of the spectrum, Scientific Reports had the lowest SJR (0.9), with a total of 30.33 cites per paper.

Table 1: Most Active Source Titles

Rank	Journal Title	Country	Paper	Citations	Cites/year	SJR 2023	Cites/paper
1	*Journal of Biological Chemistry*	United States	14	964	50.74	1.77	68.86
2	*Traffic*	Denmark	6	436	24.22	1.85	72.67
3	*Autophagy*	United States	5	173	13.31	4.04	34.60
3	*Cell Calcium*	United Kingdom	5	164	16.40	1.31	32.80
3	*Nature Communications*	United Kingdom	5	639	63.90	4.89	127.80
3	*Proceedings of The National Academy of Sciences of The United States of America*	United States	5	535	26.75	3.74	107.00
4	*Biochemical Journal*	United Kingdom	4	206	12.88	1.61	51.50
4	*Cells*	Switzerland	4	4	1.00	1.55	1.00
4	Journal of Cell Science	United Kingdom	4	122	9.38	1.59	30.50
5	*American Journal of Physiology Cell Physiology*	United States	3	88	6.77	1.71	29.33
5	*Human Mutation*	United Kingdom	3	155	6.74	1.69	51.67
5	*International Journal of Molecular Sciences*	Switzerland	3	22	5.50	1.18	7.33
5	*Nature*	United Kingdom	3	636	39.75	18.51	212.00
5	*Oxidative Medicine and Cellular Longevity*	United States	3	32	5.33	1.48	10.67

5	*Pflugers Archiv European Journal of Physiology*	Germany	3	189	9.95	1.36	63.00
5	*Scientific Reports*	United Kingdom	3	91	15.17	0.9	30.33

The top 10 highly cited documents are listed in Table 2. Among them, Xian-Ping Dong's 2008 article titled "The type IV mucolipidosis-associated protein TRPML1 is an endolysosomal iron release channel" stood out as the most cited with 429 citations. This is followed by a 2016 article by Xiaoli Zhang titled "MCOLN1 is a ROS sensor in lysosomes that regulates autophagy", which received 356 citations. The third highly cited article with 232 citations was published in 2015 and authored by Ju-Hyun Lee entitled "Presenilin 1 Maintains Lysosomal Ca^{2+} Homeostasis via TRPML1 by Regulating vATPase-Mediated Lysosome Acidification". These ten highly cited documents are original research articles.

Table 2: Ten Most Influential Articles

Title	First Author	Journal	Year	Citation Frequency	Main Conclusion
The type IV mucolipidosis-associated protein TRPML1 is an endolysosomal iron release channel	Xian-Ping Dong	Nature	2008	429	In this study they establish the role of TRPML1 in maintaining intracellular iron homeostasis. Mutational disruption of this gene can impair iron transport and contribute to the development and symptoms of ML4 patients.
MCOLN1 is a ROS sensor in lysosomes that regulates autophagy	Xiaoli Zhang	Nature Communications	2016	356	TRPML1 is the ROS sensor. The research demonstrated an alternate method of autophagy activation through an inducible process via the ROS-TFEB-TRPML1 pathway.
Presenilin 1 Maintains Lysosomal Ca^{2+} Homeostasis via TRPML1 by Regulating vATPase-Mediated Lysosome Acidification	Ju-Hyun Lee	Cell Reports	2015	232	This study found a link between TRPML1 and Ca^{2+} efflux caused by PS1 deletion. PS1KO causes the vATPase V0a1 subunit to become unstable and raises lysosomal pH, thus causing TRPML1 to release aberrant Ca^{2+} homeostasis.
Caenorhabditis elegans functional orthologue of human protein h-mucolipin-1 is required for lysosome biogenesis	Sebastian Treusch	Proceedings of the National Academy of Sciences of the United States of America	2004	197	The main goal of this paper is to illustrate the significance of CUP-5, a protein that was first discovered in Caenorhabditis elegans and is an orthologue of human h-mucolipin-1. CUP-5 proposes a functional nematode protein that can modulate CUP-5 activity, providing an understanding of how to quickly and accurately translate the

					mechanism within human mutant h-mucolipin-1 and h-mucolipin-3 proteins.
TRP-ML1 regulates lysosomal pH and acidic lysosomal lipid hydrolytic activity	Abigail A. Soyombo	Journal of Biological Chemistry	2006	195	The most important conclusion from this research is that TRPML1 can provide H+ ions, which enables it to regulate lysosomal pH as well as lipid breakdown and metabolism in a cell.
Regulation of endocytosis by CUP-5, the Caenorhabditis elegans mucolipin-1 homolog	Hanna Fares	Nature Genetics	2001	193	The ability of CUP-5 to regulate endocytosis processes is described in this paper. Human MLIV disease was not caused by lysosomal hydrolase deficiency, but rather by abnormal endocytosis activities. Cup-5 is a homolog model of human mucolipin-1, therefore using it to study the structure and function of human illnesses linked to MCOLN1 mutations may help shed light on the fundamental mechanisms involved.
Up-regulation of lysosomal TRPML1 channels is essential for lysosomal adaptation to nutrient starvation	Wuyang Wang	Proceedings of the National Academy of Sciences of the United States of America	2015	169	This study's main objective is to investigate TRPML1's capacity to control cells' responses to nutrition deprivation. Within hours of nutrition starvation or mTOR / TFEB suppression to imitate deprivation, ML1 will potently up-regulate, releasing Ca^{2+} signalling, as impulses to create the needs necessary for autophagosome and lysosome development.
Mitochondria-lysosome contacts regulate mitochondrial Ca^{2+} dynamics via lysosomal TRPML1	Wesley Peng	Proceedings of the National Academy of Sciences of the United States of America	2020	140	The paper emphasizes TRPML1's role in Ca^{2+} transfer and its relevance to lysosomal storage disorders, like mucolipidosis type IV (MLIV). MLIV features malfunctioning TRPML1 channels, altering Ca^{2+} dynamics between lysosomes and mitochondria. Patient fibroblasts with MLIV show faulty mitochondria–lysosome contact dynamics and impaired Ca^{2+} uptake, highlighting these interactions' importance in disease pathophysiology.
Two di-leucine motifs regulate trafficking of mucolipin-1 to lysosomes	Silvia Vergarajauregui	Traffic	2006	139	According to the authors' findings, two nonidentical chimaeras of the N- and C- di-leucine motif are significant modulators that physically control mucolipin-1 trafficking. The distinct activities of each terminal tail made it

					possible for mucolipin-1 to effectively modulate endocytosis and directly locate this protein in lysosomes.
Mucolipin-1 is a lysosomal membrane protein required for intracellular lactosylceramide traffic	Paul R. Pryor	Traffic	2006	137	In MLIV cells, lactosylceramide flow is significantly compromised. This study shows that the integration of mucolipin-1 expression from the wild type is the sole way to restore the function of mutant MLIV cells since mucolipin-1 can recover abnormal lactosylceramide trafficking when it is localised correctly.

3.4 Authors networking

A total of 158 writers contributed to the 155 articles on TRPML1 (Appendix D). Among these, the top 12 writers collectively contributed 61 papers (39.35%) (Table 3). Notably, Susan A Slaugenhaupt and Haoxing Xu each published 10 papers, followed by Christian Grimm and Kirill Kiselyov with 9 papers each.

In terms of citations, Haoxing Xu stood out as the most highly cited author with 1449 citations. Xiping Cheng followed with 971 citations from four articles. Markus Delling, despite having only 3 publications, ranked third with 876 citations.

Among the top ten most prolific authors, Susan A Slaugenhaupt led the way with 789 citations, securing the first rank. Xian-Ping Dong (ranked 5th, 728 citations), Kirill Kiselyov (ranked 4th, 645 citations) and Hanna Fares (ranked 7th, 547 citations) also made the list of highly referenced authors.

Table 3: Top 10 Productive Authors

	Authors	Number of papers
1)	Susan A. Slaugenhaupt	10
2)	Haoxing Xu	10
3)	Christian Grimm	9
4)	Kirill Kiselyov	9
5)	Xian-Ping Dong	8
6)	Ehud Goldin	7
7)	Hanna Fares	6
8)	Wuyang Wang	6
9)	Yiming Yang	6
10)	Franz Bracher	5
11)	Math P. Cuajungco	5
12)	Shmuel Muallem	5

	Authors	Number of citations
1)	Haoxing Xu	1449
2)	Xiping Cheng	971
3)	Markus Delling	876
4)	Susan A. Slaugenhaupt	789
5)	Xian-Ping Dong	728
6)	Qiong Gao	689
7)	Xiaoli Zhang	689
8)	Kirill Kiselyov	645
9)	Marc Ferer	620
10)	Hanna Fares	547
11)	Maria Lawas	525
12)	Juan Marugan	525

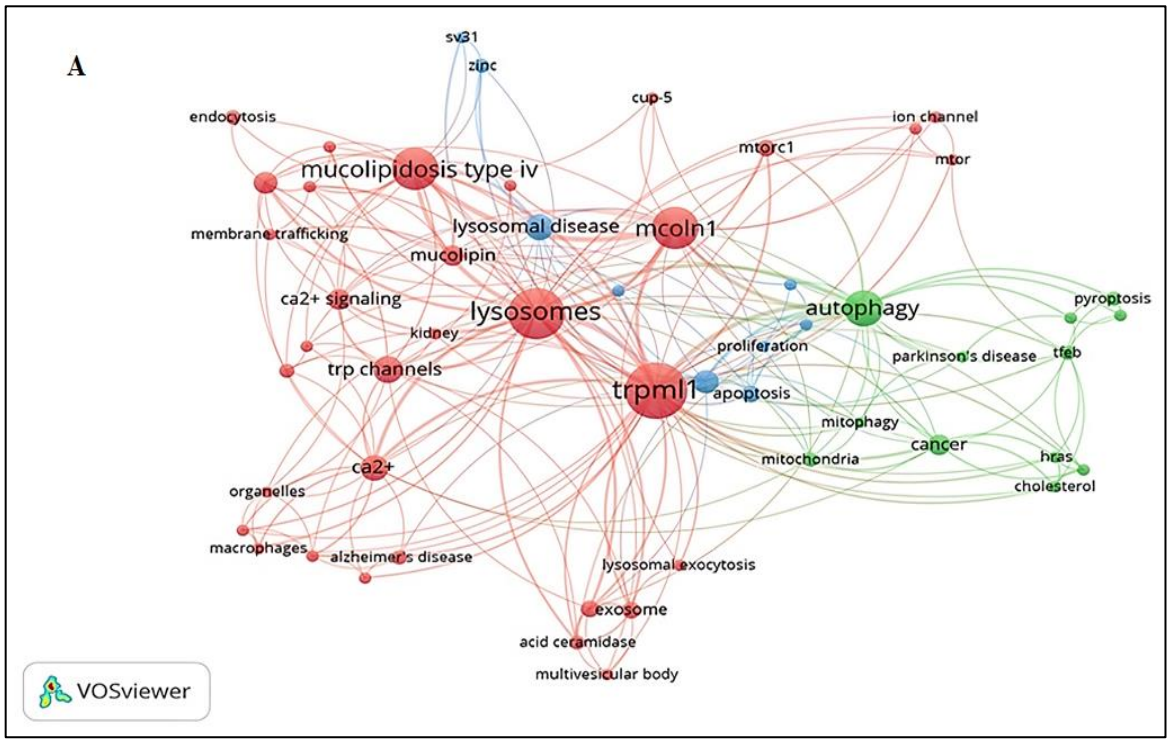
3.5 Author keywords

In this study, we employed VOSviewer to analyse the author keywords across the 155 articles. A total of 335 keywords were yielded from these articles. Among them, 54 keywords met the threshold for co-occurrences, appearing more than twice. The resulting network map (Fig. 4A) visually

illustrates the intricate relationships between these keywords.

The network map comprises nodes and connecting lines. Each node corresponds to a specific keyword, while the lines represent connections between pairs of keywords. Keywords sharing the same hue and forming clusters were indicative of frequent co-occurrence. From the authors' inputs, a total of three clusters (min. cluster size: 8.0) and 243 linkages in the keywords were derived. Cluster 1, in red hue, was the largest cluster with 33 items, mostly connected to lysosomal disorders, with TRPML1 and lysosomes having the most occurrences. Cluster 2 in green consisted of 12 keywords that were strongly associated with cellular regulations, such as autophagy and cancer. Cluster 3 in blue consisted of 9 keywords, the majority of which were associated with cellular stress, encompassing concepts such as apoptosis, lysosomal disease and ROS.

Fig. 4B represents a visual overlay generated by VOSviewer, which categorises keywords into a spectrum of hues, from cool to warm, based on their developmental age. In earlier years of TRPML1 research, terms such as endosomes and mucolipidosis type IV were prevalent, indicated by blue and cyan tints. However, recent research has predominantly focused on TRPML1, Ca^{2+}, autophagy and cancer, represented by orange and red colors.



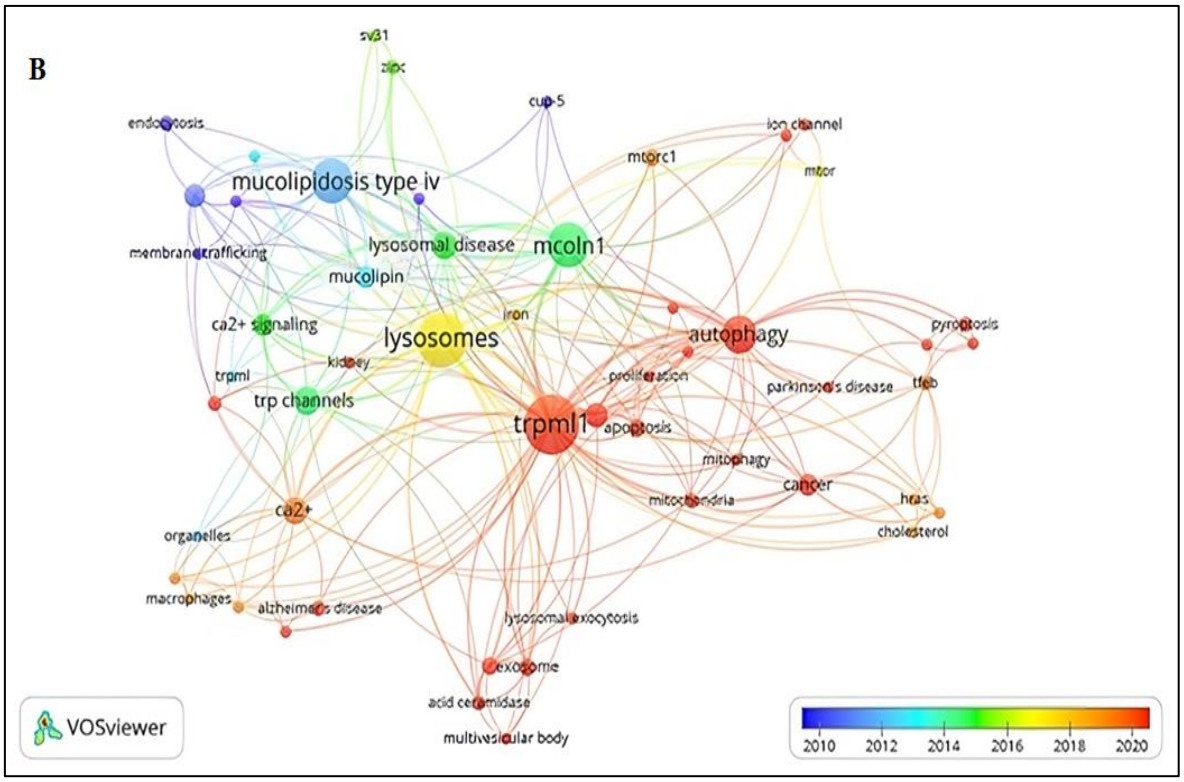


Figure 4: (A) Network Visualization Map. (B) Overlay visualization Map.

4.0 Discussion

The discussion surrounding TRPML1 research trends, citations, and document types provides crucial insights into the evolving landscape of this field over the past two decades. By analysing publication output and citation impact, we gain a nuanced understanding of the factors influencing research dissemination and scholarly recognition. The observed fluctuations in publication output, notably influenced by external events, underscore the dynamic nature of scientific inquiry. Moreover, the distribution of publication categories sheds light on the balance between original research contributions and literature synthesis within the TRPML1 domain. Delving into global citation patterns, journal distributions, highly cited articles, and authorship dynamics further enriches our understanding of the collaborative networks and influential voices driving TRPML1 research. As we explore emerging research frontiers, we identify promising avenues for future investigation, ultimately contributing to the advancement of knowledge in this vital field.

4.1 TRPML1 Publications: Trends, Citations, and Document Types

TRPML1-related publication and citation data show interesting trends. Since its inception in 2001, publication numbers have varied, peaking in 2019. They dropped sharply in 2020, likely due to the COVID-19 pandemic as observed in other unrelated studies (16) but rebounded and have been rising steadily since. The trend suggests a potential surpassing of the 2019 peak this year. Citation counts fluctuated, with peaks in 2006, 2008, 2015, and 2019 indicating influential research periods. Despite consistent publication output, citation impact declined post-2019.

The publication categories show a clear focus on original research, with "Articles" comprising 94.84%, reflecting the field's commitment to creating new insights. "Review" publications, at 5.16%, play an

important role in summarising and critiquing existing knowledge. This balance indicates a vibrant research portfolio, with a strong focus on original work and a recognition of the value of literature synthesis. The distribution invites further investigation into the relationship between publication types and citation impact. For example, years with high citations may correlate with groundbreaking articles, while review articles could help contextualise and consolidate research impact. This understanding can guide future strategies by considering both the volume and nature of publications for sustained excellence and impact.

4.2 Nations and their Impact: Citation Counts in TRPML1 Publications

The global landscape of TRPML1 research publications and citations offers intriguing insights into the collaborative and diverse nature of this scientific domain. The US emerged as a dominant contributor, evidenced by 85 publications and a substantial 5529 citations. It consistently led to publications, reaching a peak of 11 in 2019, reflecting sustained engagement and leadership in TRPML1 research. This is unsurprising, given the US' prominent role in research on Ca^{2+} channels (17) and TRP channels (18). Following the US was China with 36 publications and 1310 citations. In recent years, China has exhibited a noticeable upward trajectory, indicating an increasing prominence in the field. In 2024, China surpassed the US with 5 publications compared to 2, hinting at a potential shift in influence. Other key contributors, including Germany, Canada, and the UK, exhibited considerable activity, contributing significantly to both publications and citations.

Noteworthy was Sweden's single publication, which, despite its lower publication count, boasted an exceptionally high citation impact of 429, emphasizing the quality and influence of its research output. The research area for this paper focused on the Type IV Mucolipidosis-Associated Protein TRPML1 and its role as an endolysosomal iron release channel. The study investigates the function of TRPML1 in releasing Fe^{2+} from late endosomes and lysosomes, as well as how mutations in the TRPML1 gene contribute to the mucolipidosis type IV disease (ML4). The research delves into the cellular iron homeostasis and the potential implications for developing therapeutic interventions for ML4 patients.

This paper holds considerable influence due to several factors. Its publication in Nature, a renowned scientific journal, instantly elevates its credibility and visibility. Offering novel insights into the role of TRPML1 in maintaining intracellular iron balance, the research addresses the molecular intricacies of ML4, a rare genetic disorder. Such findings not only advance our understanding of ML4 but also offer potential avenues for therapeutic interventions, garnering attention from both researchers and clinicians. The paper's high citation frequency underscores its widespread recognition and impact within the scientific community. Furthermore, its implications extend beyond ML4, contributing to broader inquiries into cellular iron homeostasis and lysosomal function, making it relevant to a wider spectrum of scientific investigations. Overall, this distribution highlights the interconnected and impactful nature of TRPML1 research, with diverse contributions from countries enriching the global understanding of this critical topic.

4.3 Journal Distributions and Highly Cited Articles: Analysing TRPML1 Publications

Among the 5 most active journals, the Journal of Biological Chemistry stood out as a primary venue for TRPML1 research, publishing 14

articles with a remarkable average citation rate of 68.86 citations per paper, indicating its significant impact in the field. Anomalously, Cells presented a contrasting picture with only 4 papers and an average citation rate of 1.00, suggesting limited visibility or impact within the TRPML1 research community.

Further, the distribution of journals across countries revealed interesting patterns. While the US and the UK are well-represented, with multiple journals featuring prominently, Switzerland's International Journal of Molecular Sciences showcased a modest contribution, publishing 3 papers with an average citation rate of 7.33. Conversely, Nature, based in the United Kingdom, presented an outlier with only 3 papers but an exceptionally high average citation rate of 212.00, indicating the journal's strong influence despite its lower publication output in TRPML1 research.

Additionally, the disparity in citation rates among journals underscored the multifaceted nature of TRPML1 literature dissemination. For instance, while Traffic, based in the UK, published 6 papers, its high average citation rate of 72.67 reflected the journal's impact and relevance within the TRPML1 research community. In contrast, Scientific Reports, also based in the UK, presented a noteworthy anomaly with 3 papers but a relatively lower average citation rate of 30.33, signalling potential variations in the journal's perceived significance or readership engagement within the field.

The Journal of Biological Chemistry, boasting the largest number of published TRPML1 papers, exclusively features research articles within the realms of Biochemistry, Genetics, and Molecular Biology. In contrast, Nature, despite its infrequent publication output in these areas, stands out for its high citation rates in TRPML1 research. Nature's multidisciplinary approach covers subjects such as the structure of the TRPML1 channel and Mucolipidosis Type IV, appealing to a wide range of researchers. Nature likely has higher citation rates because it is known for publishing groundbreaking research that grabs the attention of the scientific community worldwide. Its stringent selection criteria ensure that only the best and most innovative research gets published. Additionally, Nature's strong reputation, broad readership, and global visibility mean that papers published there are widely noticed and cited. Overall, Nature's prestige, quality standards, and wide reach help explain why its papers tend to receive more citations than those in the Journal of Biological Chemistry.

Overall, these irregularities highlight the nuanced dynamics underlying journal contributions and citation patterns within the TRPML1 research domain. While certain journals emerge as key dissemination channels with significant impact, differences in publication output and citation rates prompt further exploration into factors influencing journal selection and readership engagement within the TRPML1 research community.

4.4 Key Insights Unveiled: Exploring the Significance of the Ten Most Influential TRPML1 Articles

The top 10 highly cited documents in TRPML1 research provide significant insights into the pivotal findings within this field. Topping the list was Xian-Ping Dong's seminal 2008 article titled "The type IV mucolipidosis-associated protein TRPML1 is an endolysosomal iron release channel," which garnered an impressive 429 citations. Following closely was Xiaoli Zhang's 2016 article "MCOLN1 is a ROS sensor in lysosomes that regulates autophagy," with 356 citations, and Ju-Hyun Lee's 2015 publication "Presenilin 1 Maintains Lysosomal Ca^{2+} Homeostasis via TRPML1 by Regulating vATPase-Mediated Lysosome Acidification," cited

232 times. Notably, these highly cited articles encompass a range of topics, from elucidating TRPML1's role in intracellular iron homeostasis to its regulation of lysosomal Ca^{2+} dynamics and ROS-mediated autophagy induction.

Irregularities within this list are evident in the publication venues and citation frequencies. For instance, while Dong's article is published in the prestigious journal Nature, it is remarkable that the article in the journal Traffic by Silvia Vergarajauregui, "Two di-leucine motifs regulate trafficking of mucolipin-1 to lysosomes," received 139 citations, which is comparatively high considering its publication in a lesser-known journal. Additionally, the discrepancy in citation counts across articles highlights the varying degrees of impact and significance within TRPML1 literature. While some articles, like Dong's, enjoy widespread recognition and citations, others, despite being published in renowned journals, may receive comparatively fewer citations, indicating potential gaps in visibility or dissemination.

This evaluation helps researchers make more informed choices about where to submit their work, balancing between high-impact journals and those that offer wider dissemination within the relevant research community. These irregularities underscore the multidimensional nature of scholarly impact and the diverse pathways through which groundbreaking research can be disseminated and recognised within the scientific community. Further exploration of the factors contributing to these irregularities can offer valuable insights into the dynamics of knowledge dissemination and the mechanisms driving scholarly recognition within TRPML1 research.

4.5 Authorship Dynamics in TRPML1 Research: Patterns and Insights

In the landscape of TRPML1 research, a comprehensive analysis of authorship patterns reveals both notable trends and intriguing irregularities. A total of 158 authors collectively contributed to 155 articles, forming a dynamic network of scholarly collaboration. However, the top 12 prolific authors, responsible for 39.35% of the papers, showcase interesting dynamics in their publication and citation metrics.

Susan A Slaugenhaupt and Haoxing Xu were the most prolific authors, each contributing 10 papers. However, despite this, only Haoxing Xu made it to the top three most highly cited authors, amassing a significant 1449 citations. In contrast, Xiping Cheng, with only four article papers, secured the second-highest citations (971), while Markus Delling, ranked third with 876 citations from just three published documents. This discrepancy in citation counts among prolific authors emphasises the nuanced nature of scholarly impact, where the number of publications does not always correlate directly with citation success.

Interestingly, some authors with a lower publication count garnered significant citations, challenging traditional metrics of productivity. Notably, Xian-Ping Dong (ranked 5th, 728 citations), Kirill Kiselyov (ranked 4th, 645 citations), and Hanna Fares (ranked 7th, 547 citations) stood out among the top ten most prolific authors who also made the list of highly referenced contributors. This variation suggests that certain authors, despite a more modest publication output, have made substantial and impactful contributions to TRPML1 literature.

In the context of collaborative research, understanding these divergences is crucial for comprehending the intricate dynamics of author networks, influence, and the factors that contribute to scholarly recognition within the TRPML1 research community. Susan A. Slaugenhaupt and Haoxing Xu have no record of prior collaboration. Slaugenhaupt's most productive publication years were 2004, 2009, and 2010, each with two

publications. She has engaged in collaborative research with authors from the United States, Australia, and France. Notably, her most cited work, published in 2004, is titled "Caenorhabditis elegans functional orthologue of human protein h-mucolipin-1 is required for lysosome biogenesis." Her research encompasses various fields, including biochemistry, genetics, molecular biology, medicine, neuroscience, and multidisciplinary studies. Over the years, Slaugenhaupt's research focus has transitioned from the MCOLN1 gene and its chromosomal roles to studying channels, proteins, gene functions, TRPML2, and macroautophagy, before returning to research on zinc, proteins, and channels.

Haoxing Xu is a distinguished and highly cited researcher in the field of TRPML1. His peak publication year was in 2014, with three articles. Xu has collaborated twice with Xian-Ping Dong, the author of the most cited paper on TRPML1. Throughout his research on TRPML1, Xu has collaborated with authors from various countries, including the United States, China, Canada, Japan, and Sweden. His research interests span a wide range of disciplines, including biochemistry, multidisciplinary studies, chemistry, physics and astronomy, neuroscience, and pharmacology, toxicology, and pharmaceutics. Xu's research trajectory in TRPML1 has evolved from studies on MLIV and MCOLN1 to exploring recent advances in TRPML1 channels, with a focus on Ca^{2+} and Zn^{2+}, and more recently, investigations into autophagy and cancer.

Haoxing Xu likely has a higher number of citations than Susan A. Slaugenhaupt due to several factors. Xu's research on TRPML1, particularly in the context of autophagy and cancer, addresses high-impact and trending topics in biomedical research, leading to greater interest and citations. His prolific output, especially in his peak year of 2014, also contributes to his citation count. Additionally, Xu's extensive collaborations with researchers from high-research-output countries and with highly cited authors like Xian-Ping Dong enhance the visibility and dissemination of his work. In contrast, while Slaugenhaupt's research is significant, it may not intersect with as many high-interest areas or involve as extensive a network of collaborators, resulting in fewer citations. Further exploration of these patterns can provide valuable insights into the multifaceted nature of authorship and impact in this specific field.

4.6 Unlocking Insights: Navigating the Maze of Author Keywords

Analysing the evolution of research themes over time offers valuable insights into the changing landscape of scholarly inquiry. Tracking trends in research topics allows researchers to identify emerging areas of interest and understand shifts in focus, providing a comprehensive view of the progression of knowledge (19). The study using VOSviewer to analyse keywords across 155 articles exemplifies this process, revealing how research themes evolve. By identifying keyword clusters and their relationships, the study visually represents the interconnectedness of different concepts within the TRPML1 research domain.

Furthermore, categorising keywords by their developmental age illustrates temporal trends in research themes. This approach shows the transition from earlier prevalent themes, such as endosomes and mucolipidosis type IV, to more recent focuses like TRPML1, Ca^{2+}, autophagy, and cancer. These insights highlight the dynamic nature of scholarly inquiry and the continuous development of knowledge within the field. Understanding these trends guides future research directions and contributes to the advancement of the field.

The shift in research themes is driven by technological advancements, evolving societal needs, and new research methodologies. Additionally, addressing complex societal challenges increasingly requires interdisciplinary approaches and collaboration with external decision-makers to ensure research is practical and relevant. Recognising the limitations of traditional methods, there is also a growing emphasis on innovative and participatory approaches, which involves stakeholders and considers the broader implications of research in decision-making processes (20).

4.7 TRPML1 Frontiers

Keywords play a crucial role in encapsulating the essence of a research paper. They allow readers to locate, explore, and potentially cite scholarly work. Our analysis identified seven primary research frontiers of TRPML1: podocyte, exosome, and neurodegeneration in cluster 1; autophagy and cancer in cluster 2; and apoptosis and ROS in cluster 3, with an average publication year ranging from 2020 to recent. Within these TRPML1-related studies, autophagy (total link strength: 49; 45 published documents) and cancer (total link strength: 22; 18 published documents) stand out as crucial topics of investigation, indicating their significant impact on research inquiry. Further insights into these research areas are provided below.

4.7.1 TRPML1 and podocyte

Podocytes are 83pecialized cells within the kidney glomerulus that play an important function in preventing plasma proteins from entering the urine ultrafiltrate. They achieve this by establishing a barrier with the surrounding cells of the Bowman's capsule (21). Recent research has sparked interest in unravelling the connection between TRPML1 and podocytes. One study examined the effect of Asah1 gene deletion in podocytes on TRPML1 channel function. The results revealed signs of dysregulation, hinting at possible implications (22). Another study looked into the critical role of acid ceramidase in regulating TRPML1 channel-mediated Ca^{2+} release, lysosome-MVB interaction, and exosome release in podocytes (23). Additionally, a different investigation focused on the influence of NADPH oxidase-produced ROS on exosome production from podocytes. These findings suggest a potential link to inflammatory processes (24). Collectively, these investigations shed light on the complex interplay between TRPML1 channel and podocytes, underlining their importance in cellular function and disease development. However, there remains a research gap regarding the downstream implications of TRPML1 dysregulation on podocyte physiology and its relevance to kidney disease. Further research in this area may lead to the development of novel therapeutic techniques targeting TRPML1 channel in podocytes and related diseases.

4.7.2 TRPML1 and exosome

The intricate interplay between TRPML1 channel and exosome release holds significant implications for intercellular communication and disease investigation. Previous studies have meticulously examined how TRPML1 channel regulates lysosomal function and Ca^{2+} release, directly impacting exosome release (23). Notably, by blocking TRPML1 channel or inhibiting acid ceramidase, the delicate interplay between lysosomes and multivesicular bodies was disrupted, resulting in a notable increase in exosome emission (23). Moreover, TRPML1 also plays a pivotal role in the fusion of late endosomes to lysosomes, a process essential for exosome release (25).

Recent studies shed light on the complicated dynamics governing

TRPML1 channel, lysosomal function, and exosome release. These investigations highlighted the influence of ROS on TRPML1 channel function, thereby altering exosome release (26). ROS, particularly, have been linked to inflammatory exosome production via TRPML1 channel, impacting key cellular processes and inflammatory responses in podocytes.

However, despite remarkable progress, the detailed mechanisms governing TRPML1-mediated exosome release remain incompletely elucidated. Further investigation is crucial to decode the intricate signalling pathways implicated and understand their roles in various diseases. Bridging this knowledge gap holds the potential to advance the development of novel therapeutic strategies targeting TRPML1 channels and exosome release in diseases linked to podocytes.

4.7.3 TRPML1 and neurodegeneration

Neurodegenerative disorders, with Alzheimer's disease (AD) at the forefront, pose significant challenges due to their escalating prevalence, especially among aging populations. In this intricate landscape of neurodegeneration, TRPML1 channel emerges as a potential therapeutic target. Key research has 84 mphasized TRPML1's importance as a master regulator of the endosomal-autophagic-lysosomal (EAL) system, revealing its involvement in neurodegenerative processes. Notably, investigations have identified links between TRPML1 deficiencies and EAL system abnormalities in AD, particularly in APOE-ε4 iPSC-derived neurons (27). Additionally, recent studies have highlighted the promising ability of TRPML1 agonists like ML-SA1 to reverse AD-related changes in the EAL system, positioning TRPML1 as a compelling target for neurodegenerative conditions.

Furthermore, emerging research has explored TRPML1's role in Ca^{2+}-mediated stress-induced neurodegenerative diseases, including Alzheimer's, Parkinson's disease, and amyotrophic lateral sclerosis (ALS) (28). Dysfunctions in lysosomes, oxidative stress, and Ca^{2+} balance, coupled with TRPML1 activity, contribute significantly to the pathogenesis of these disorders. However, despite notable progress, a significant gap in research remains regarding the comprehensive understanding of TRPML channels' contributions to neurodegeneration and their potential therapeutic applications.

Thorough investigation is crucial to uncover the complex mechanisms underlying TRPML channels' involvement in neurodegenerative diseases. Bridging this research gap offers promising opportunities for developing innovative therapeutic approaches targeting TRPML1 channel and advancing our understanding of the mechanisms and treatment avenues for neurodegenerative disorders.

4.7.4 TRPML1 and autophagy

Autophagy, a cellular mechanism crucial for degrading and recycling dysfunctional cellular components through autophagosomes, serves to enhance cell efficiency and prevent damage accumulation, especially during periods of stress or nutrient scarcity (29). Notably, TRPML1 emerges as a significant pharmaceutical target for oncogenic autophagy across various cancer types, including pancreatic cancer, breast cancer, gastric cancer, malignant melanoma, and glioma (30). Its involvement in mediating zinc influx into the cytosol, finely tuning oncogenic autophagy by influencing fusion between autophagosomes and lysosomes (30).

Moreover, TRPML1 regulates autophagy through multiple pathways, including the CaMKKβ/VPS34 pathway, which links lysosomal Ca^{2+} to autophagosome biogenesis

(31). Recent studies have further elucidated TRPML1's role in stress-induced autophagy and its contribution to maintaining mitochondrial Ca^{2+} dynamics in non-malignant cells while stimulating autophagy in cancer cells (32). Additionally, TRPML1 activation facilitates the maturation of α-synuclein-containing autophagosomes, underscoring its significance in promoting autophagy and cellular component clearance (33).

Despite notable progress in comprehending TRPML1-mediated regulation of autophagy, numerous research gaps remain. The intricate mechanisms governing TRPML1's role in autophagy regulation, especially concerning different cancer types, are not yet fully understood. Further exploration is necessary to untangle these complexities and leverage TRPML1 as a potential therapeutic target for modulating autophagy in cancer and other diseases.

4.7.5 TRPML1 and cancer

The investigation into TRPML1's involvement in cancer has revealed a complex and context-dependent impact across diverse cancer types. In this section, we delve into the nuanced role of TRPML1 in cancer advancement. Notably, TRPML1 demonstrates heightened expression in non-small-cell lung cancer and triple-negative breast cancer (TNBC), correlating with advanced tumour stages, increased proliferation, migration, and invasion (34). In pancreatic ductal adenocarcinoma (PDAC), elevated TRPML1 levels predict unfavourable clinical outcomes, including diminished overall survival. Moreover, TRPML1 plays a crucial role in maintaining oncogenic HRAS at the plasma membrane through the regulation of cholesterol homeostasis in cancer cells harbouring oncogenic HRAS mutations, rendering them more vulnerable to TRPML1 inhibition (35).

However, TRPML1's impact on cancer progression extends beyond straightforward promotion or inhibition. In glioblastoma, TRPML1 induces autophagic cell death rather than promoting oncogenesis (34). Furthermore, the expression patterns and functional effects of TRPML1 vary significantly among different cancer types, necessitating careful consideration of its specific role in each tumour. Despite notable advancements, there remains a substantial research gap in fully understanding the complex mechanisms underlying TRPML1's influence on cancer progression.

Ongoing research endeavours strive to unravel the intricate dynamics between TRPML1 and cancer. By gaining comprehensive understanding of TRPML1's role, we can inform innovative therapeutic strategies targeting this channel across diverse tumour types. Nevertheless, further exploration is imperative to develop efficacious therapeutic interventions.

4.7.6 TRPML1 and apoptosis

Apoptosis, a fundamental process in programmed cell death, plays a crucial role in eliminating unnecessary or damaged cells throughout an organism's lifecycle (36). TRPML1 is implicated in apoptosis through its regulation of autophagy. Recent studies suggest that TRPML1-induced autophagy inhibition contributes to mitochondrial dysfunction, leading to increased production of ROS, DNA damage, and subsequent activation of p53, ultimately promoting mitochondrial-mediated apoptosis in cancer cells such as melanoma and glioblastoma (37). Conversely, the synthetic agonist ML-SA1 activation of TRPML1 has been found to alleviate apoptosis in photoreceptor cells following retinal detachment (RD) by mitigating excessive ROS levels and enhancing autophagy (38).

Importantly, mutations in TRPML1 affecting chloride ion binding have been observed to cause lysosomal depletion and

apoptosis under conditions of low chloride concentrations (39). In summary, TRPML1's role in apoptosis is multifaceted, encompassing both direct and indirect mechanisms in the regulation of cell survival and death.

In spite of significant advancements in understanding TRPML1's involvement in apoptosis, several research gaps persist. Further exploration is needed to elucidate the intricate molecular mechanisms underlying TRPML1-mediated apoptosis regulation, particularly in various cancer types and under different physiological conditions. Additionally, more studies are warranted to uncover potential therapeutic strategies targeting TRPML1 to modulate apoptosis, thereby offering new avenues for the treatment of apoptosis-related disorders and diseases.

4.7.7 TRPML1 and ROS

ROS are oxygen-containing molecules that are highly reactive, playing pivotal roles in cell signalling and maintaining cellular balance. However, when present in excess, they can lead to oxidative stress and cellular damage (40). TRPML1 assumes a critical role in responding to ROS within lysosomes. When ROS activate TRPML1 channel, it triggers the release of Ca^{2+} from lysosomes, initiating autophagy induction and lysosome biogenesis through the activation of TFEB. Conversely, inhibiting or genetically deactivating TRPML1 impairs the clearance of damaged mitochondria and excess ROS (41). This interaction between TRPML1 and ROS is indispensable for various cellular processes, including autophagy, lysosome biogenesis, and stress response mechanisms (31). Furthermore, studies suggest that ROS produced within cells can modulate TRPML1 channel activity, thereby influencing processes like exosome secretion and cancer metastasis (24).

The discussion revolves around the intricate interplay between TRPML1 and ROS, highlighting their essential roles in cellular function and disease development. Key research works underscore TRPML1's capacity to respond to ROS within lysosomes, governing critical cellular processes such as autophagy and lysosome biogenesis. Recent investigations shed light on the modulation of TRPML1 channel activity by endogenously produced ROS, implicating TRPML1 in processes like exosome secretion and cancer metastasis.

Nevertheless, despite progress, there are still several areas of research that remain unexplored. Additional investigation is needed to gain a complete understanding of the molecular mechanisms involved in the interaction between TRPML1 and ROS, especially concerning disease pathogenesis. Furthermore, exploring the therapeutic possibilities of targeting TRPML1-ROS interactions could introduce innovative approaches to managing conditions linked to oxidative stress and disturbances in cellular balance.

5.0 Conclusion

In this article, we present a comprehensive bibliometric analysis of TRPML1 research, a tool that is invaluable for understanding research trends and impact. However, it is important to acknowledge that these studies are not without their limitations. They often depend on specific databases, each with its own coverage and indexing criteria, potentially leading to incomplete or biased datasets. The influence of self-citations and the variance in citation practices across disciplines can also skew the perceived impact of research. Additionally, raw citation counts do not capture the context and reasons behind citations, and bibliometric studies may overlook qualitative aspects of research impact, such as policy influence and societal benefits.

Despite these limitations, our study has uncovered significant trends and patterns in publication output, citation counts, and authorship dynamics within the realm of TRPML1 research. By grasping these insights, researchers can identify key areas for focus and foster collaborative efforts, thereby amplifying the impact of forthcoming studies.

Our exploration of TRPML1's multifaceted role, spanning podocyte function, exosome release, neurodegeneration, autophagy regulation, cancer progression, apoptosis, and ROS interaction, provides critical insights into fundamental cellular processes and disease mechanisms. While significant progress has been made in understanding TRPML1 across various research fronts, several gaps persist, warranting further investigation to unravel complexities and develop effective therapeutic strategies targeting TRPML1 dysregulation.

Additionally, our analysis sheds light on the global landscape of TRPML1 research, highlighting contributions from different countries and journals. By synthesising this multifaceted analysis, our study aims to inspire further exploration and innovation in TRPML1 research, ultimately advancing biomedical science and healthcare.

While our bibliometric analysis provides a map of the current research landscape and practical guidance for strategic focus of research efforts, it is crucial to interpret these studies with an understanding of their limitations. A more balanced view can be achieved by supplementing them with qualitative assessments. This approach will enable researchers, institutions, and policymakers to allocate funding and support impactful research initiatives effectively.

Authorship contribution statement

LIAM: Writing - original draft preparation, data preparation and analysis; **AHJ:** Conceptualization, writing – review and editing, data analysis; **MHH**: writing – review and editing.

Acknowledgment

The authors acknowledge the Ministry of Higher Education Malaysia (MoHE) and Universiti Teknologi MARA (UiTM), Malaysia for funding this study through the Fundamental Research Grant Scheme (FRGS) (FRGS/1/2019/SKK09/UITM/03/1), Lestari (600-IRMI/FRGS 5/3/LESTARI (014/2019)) and *Geran Intensif Pelajar (GIP)* (600-RMC/GIP 5/3 (044/2022)).

Conflict of Interest

The authors declared that they have no conflicts of interest to disclose.

References

1. Siow WX, Kabiri Y, Tang R, Chao Y-K, Plesch E, Eberhagen C, et al. Lysosomal TRPML1 regulates mitochondrial function in hepatocellular carcinoma cells. J Cell Sci 2022;135(6): jcs259455.

2. Schwartz DM, Muallem S. Oncogenes calling on a lysosomal Ca2+ channel. EMBO Rep 2019;20(4): e47953.

3. Minckley TF, Zhang C, Fudge DH, Dischler AM, LeJeune KD, Xu H, et al. Sub-nanomolar sensitive GZnP3 reveals TRPML1-mediated neuronal Zn2+ signals. Nat Commun 2019;10(1):4806.

4. Peng W, Wong YC, Krainc D. Mitochondria-lysosome contacts regulate mitochondrial Ca2+ dynamics via lysosomal TRPML1. Proc Natl Acad Sci U S A 2020; 117:19266-19275.

5. Sun X, Xu M, Cao Q, Huang P, Zhu X, Dong X-P. A lysosomal K+ channel regulates large particle phagocytosis by facilitating lysosome Ca2+ release. Sci Rep 2020; 10:1038.

6. Scotto Rosato A, Montefusco S, Soldati C, Di Paola S, Capuozzo A, Monfregola J, et al. TRPML1 links lysosomal calcium to autophagosome biogenesis through the activation of the CaMKKβ/VPS34 pathway. Nat Commun 2019; 10:5630.

7. Griffin CS, Alvarado MG, Yamasaki E, Drumm BT, Krishnan V, Ali S, et al. The intracellular Ca2+ release channel TRPML1 regulates lower urinary tract smooth muscle contractility. Proc Natl Acad Sci U S A 2020; 117:30775-30786.

8. Goodridge JP, Jacobs B, Saetersmoen ML, Clement D, Hammer Q, Clancy T, et al. Remodeling of secretory lysosomes during education tunes functional potential in NK cells. Nat Commun 2019;10(1):514.

9. Tedeschi V, Petrozziello T, Sisalli MJ, Boscia F, Canzoniero LMT, Secondo A. The activation of Mucolipin TRP channel 1 (TRPML1) protects motor neurons from L-BMAA neurotoxicity by promoting autophagic clearance. Sci Rep 2019;9(1):10743.

10. Kasitinon SY, Eskiocak U, Martin M, Bezwada D, Khivansara V, Tasdogan A, et al. TRPML1 promotes protein homeostasis in melanoma cells by negatively regulating MAPK and mTORC1 signaling. Cell Rep 2019; 28:2293-2305.

11. Murnaka NP. Educational technology research trends: A bibliometrics analysis and visualization. Turk J Comput Math Educ 2021; 12:2695-2701.

12. Yang KH, Thoo AC. An exploration of trends and future directions in sustainability performance: A bibliometric analysis of Scopus database. F1000Res 2022; 11:864.

13. Ng JY, Liu H, Shah AQ, Wieland LS, Moher D. Characteristics of bibliometric analyses of the complementary, alternative, and integrative medicine literature: A scoping review protocol. F1000Res 2023; 12:164.

14. Metinal YB, Gumusburun Ayalp G. Effects of the COVID-19 pandemic on architectural education: Bibliometric and content analyses. Open House Int 2022; 47:657-687.

15. Rufaida Z, Nandiyanto ABD. Bibliometric analysis of aluminium oxide nanoparticle in biomedical applications. Adv Sustainable Sci Eng Technol 2022; 4:0220203.

16. Jamaludin SYN, Jahidin AH, Zakaria R. Bibliometric analysis and review of research frontiers on transient receptor potential vanilloid 4 channels. Biomed Res Ther 2023;5671-5679.

17. Shi J, Wang H, Shi S, Yuan G, Jia Q, Shi S, et al. Bibliometric analysis of calcium channel research (2010–2019). Channels 2020; 14:193-202.

18. Zhu X, Tian C, Zhou Y, Shi J, Yuan G, Zhang L, et al. Transient receptor potential channels: A global bibliometric analysis from 2012 to 2021. Channels 2021; 15:624-634.

19. Xu M, Du J, Xue Z, Guan Z, Kou F, Shi L. A scientific research topic trend prediction model based on multi-LSTM and graph convolutional network. Int J Intell Syst 2022; 37:6331-6353.

20. Wowk K, McKinney L, Muller-Karger F, Moll R, Avery S, Escobar-Briones E, et al. Evolving academic culture to meet societal needs. Palgrave Commun 2017; 3:35.

21. Garg P. A review of podocyte biology. Am J Nephrol 2018; 47:3-13.

22. Li G, Huang D, Bhat OM, Poklis JL, Zhang A, Zou Y, et al. Abnormal podocyte TRPML1 channel activity and exosome release in mice with podocyte-specific Asah1 gene deletion. Biochim Biophys Acta Mol Cell Biol Lipids 2021; 1866:158856.

23. Li G, Huang D, Hong J, Bhat OM, Yuan X, Li P-L. Control of lysosomal TRPML1 channel activity and exosome release by acid ceramidase in mouse podocytes. Am J Physiol Cell Physiol 2019;317

24. Li G, Huang D, Li N, Ritter JK, Li P-L. Regulation of TRPML1 channel activity and inflammatory exosome release by endogenously produced reactive oxygen species in mouse podocytes. Redox Biol 2021; 43:102013.

25. Kim MS, Muallem S, Kim SH, Kwon KB, Kim MS. Exosomal release through TRPML1-mediated lysosomal exocytosis is required for adipogenesis. Biochem Biophys Res Commun 2019; 510:409-415.

26. Li G, Zhang Q, Yuan X, Li P. Enhanced exosome release and inhibited TRPML1 channel activity in podocytes from mice with podocyte-restricted deletion of Asah1 gene. FASEB J 2019;33(1):716.4-716.4.

27. Somogyi A, Kirkham ED, Lloyd-Evans E, Winston J, Allen ND, Mackrill JJ, et al. The synthetic TRPML1 agonist ML-SA1 rescues Alzheimer-related alterations of the endosomal-autophagic-lysosomal system. J Cell Sci 2023;136(6): jcs259875.

28. Santoni G, Maggi F, Amantini C, Marinelli O, Nabissi M, Morelli MB. Pathophysiological role of transient receptor potential mucolipin channel 1 in calcium-mediated stress-induced neurodegenerative diseases. Front Physiol 2020;11:1-10.

29. Shabkhizan R, Haiaty S, Moslehian MS, Bazmani A, Sadeghsoltani F, Saghaei Bagheri H, et al. The beneficial and adverse effects of autophagic response to caloric restriction and fasting. Adv Nutr 2023; 14:1211-1225.

30. Qi J, Xing Y, Liu Y, Wang MM, Wei X, Sui Z, et al. MCOLN1/TRPML1 finely controls oncogenic autophagy in cancer by mediating zinc influx. Autophagy 2021; 17:4401-4422.

31. Scotto Rosato A, Montefusco S, Soldati C, Di Paola S, Capuozzo A, Monfregola J, et al. TRPML1 links lysosomal calcium to autophagosome biogenesis through the activation of the CaMKKβ/VPS34 pathway. Nat Commun 2019;10(1):5630

32. Yang Y, Zhai X, El Hiani Y. TRPML1—Emerging roles in cancer. Cells 2020; 9:2682.

33. Pollmanns MR, Beer J, Rosignol I, Rodriguez-Muela N, Falkenburger BH, Dinter E. Activated endolysosomal cation channel TRPML1 facilitates maturation of α-synuclein-containing autophagosomes. Front Cell Neurosci 2022; 16:861202

34. Xu M, Dong XP. Endolysosomal TRPMLs in cancer. Biomolecules 2021; 11:65.

35. Jung J, Cho K, Naji AK, Clemons KN, Wong CO, Villanueva M, et al. HRAS-driven cancer cells are vulnerable to TRPML1 inhibition. EMBO Rep 2019;20(4): e46685

36. Krasovec G, Horkan HR, Quéinnec É, Chambon JP. The constructive function of apoptosis: More than a dead-end job. Front Cell Dev Biol 2022; 10:1033645

37. Liu Y, Wang X, Zhu W, Sui Z, Wei X, Zhang Y, et al. TRPML1-induced autophagy inhibition triggers mitochondrial mediated apoptosis. Cancer Lett 2022; 541:215752.

38. Yan Y, Wang Y, Ding J, Lu L, Ke GJ, Dong K. TRPML1 inhibited photoreceptor apoptosis and protected the retina by activation of autophagy in experimental retinal detachment. Ophthalmic Res 2020; 64:587-594.

39. Lee D, Hong JH. Modulation of lysosomal Cl− mediates migration and apoptosis through the TRPML1 as a lysosomal Cl− sensor. Cells 2023; 12:1835.

40. Sies H, Belousov VV, Chandel NS, Davies MJ, Jones DP, Mann GE, et al. Defining roles of specific reactive oxygen species (ROS) in cell biology and physiology. Nat Rev Mol Cell Biol 2022; 23:499-515.

41. Clement D, Szabo EK, Krokeide SZ, Wiiger MT, Vincenti M, Palacios D, et al. The lysosomal calcium channel TRPML1 maintains mitochondrial fitness in NK cells through interorganelle cross-talk. J Immunol 2023; 211:1348-1358.