Araştırma Makalesi – Original Article

Global Collaborations in SREBP Research: Scientific Productivity and Impact *

SREBP Araştırmalarında Küresel İş birlikleri: Bilimsel Üretkenlik ve Etki

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ÖZ

Amaç: Bu çalışma, SREBP araştırmalarının bilimsel etkisini ve zaman içindeki gelişimini değerlendiren kapsamlı bir bibliyometrik analiz sunmaktadır. Sterol düzenleyici element bağlayıcı proteinler (SREBP'ler) lipid sentezini ve alımını düzenleyen transkripsiyon faktörleridir. Lipogenez, endoplazmik retikulum stresi, inflamasyon, otofaji ve apoptozda hayati rol oynarlar.

Yöntem: Web of Science Core Collection veri tabanını kullanarak 1997'den 2024'e kadar yayınlanmış orijinal araştırma makalelerini analiz ettik. Veri analizi VOSviewer, Bibliometrix, Biblioshiny ve Microsoft Excel kullanılarak gerçekleştirilmiş ve yayın çıktıları, ülkeler, kurumlar, dergiler, yazarlar, anahtar kelimeler ve atıflar incelenmiştir.

Bulgular: 13.910 araştırmacı tarafından yazılmış toplam 3.863 makale tespit edilmiştir. En üretken ülkeler Çin, ABD ve Güney Kore olurken, toplam atıflarda ABD başı çekmiştir. Seul Ulusal Üniversitesi ve Nanjing Tarım Üniversitesi kilit kurumlar olarak belirlenmiştir. Analiz, önemli küresel iş birliklerini ortaya çıkarmış ve SREBP'nin metabolik hastalıklar ve kanser biyolojisi üzerindeki etkisini vurgulamıştır.

Sonuç: Bu bibliyometrik analiz, SREBP araştırmalarına ilişkin değerli bilgiler sunmakta, önde gelen katkıda bulunanları, eğilimleri ve gelecekteki araştırma yönlerini belirlemektedir. Araştırmacılar için uygun dergileri, işbirlikçileri ve odak alanlarını seçmede bir rehber görevi görmektedir.

Anahtar Kelimeler: SREBP, Bibliyometrik analiz, Lipit metabolizması, Transkripsiyon faktörleri, VOSviewer.

ABSTRACT

Aim: This study provides a comprehensive bibliometric analysis of SREBP research, assessing its scientific impact and evolution over time. Sterol regulatory element-binding proteins (SREBPs) are transcription factors regulating lipid synthesis and uptake. They play vital roles in lipogenesis, endoplasmic reticulum stress, inflammation, autophagy, and apoptosis.

Methods: We analyzed original research articles published from 1997 to 2024 using the Web of Science Core Collection database. Data analysis was performed using VOSviewer, Bibliometrix, Biblioshiny, and Microsoft Excel, examining publication outputs, countries, institutions, journals, authors, keywords, and citations.

Results: A total of 3,863 articles were identified, authored by 13,910 researchers. The most productive countries were China, the USA, and South Korea, with the USA leading in total citations. Seoul National University and Nanjing Agricultural University were identified as key institutions. The analysis revealed significant global collaborations and emphasized SREBP's impact on metabolic diseases and cancer biology.

Conclusion: This bibliometric analysis offers valuable insights into SREBP research, identifying leading contributors, trends, and future research directions. It serves as a guide for researchers in selecting appropriate journals, collaborators, and focus areas.

Keywords: SREBP, Bibliometric analysis, Lipid metabolism, Transcription factors, VOSviewer

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Introduction

Fatty acids and cholesterol are crucial lipids that form the fundamental structure of cellular membranes. Their derivatives serve as significant signaling molecules that regulate cellular functions.[1] Sterol regulatory element-binding proteins (SREBPs) are a transcription factor family with a basic helix-loop-helix leucine zipper (bHLH-LZ) domain that regulates genes involved in lipid synthesis and uptake pathways. Three SREBP isoforms, SREBP-1a, SREBP-1c, and SREBP-2, derived from two genes, SREBF1 and SREBF2, have been found in mammalian cells. These isoforms have overlapping transcriptional pathways for lipid and cholesterol production.[2]

Over the past three decades, SREBPs have been found to integrate multiple cellular signals. Their versatility enables regulation of not only lipogenesis but also other processes such as ER stress, apoptosis, and autophagy.[3]

Their pivotal role in metabolic homeostasis makes them a key focus of research in metabolic disorders such as obesity, diabetes, and cardiovascular diseases.[4]

The regulatory mechanisms of SREBPs involve complex processes of cleavage and activation. In response to lipid deprivation, SREBPs are transported from the ER to the Golgi apparatus where they are cleaved by site-1 protease (S1P) and site-2 protease (S2P).[5] The mature form then translocates to the nucleus to activate target gene transcription. This process is tightly regulated by intracellular lipid levels, ensuring that lipid synthesis and uptake are balanced according to cellular needs.[6]

Bibliometric analysis is a useful tool for graphically calculating the effect of academic achievements and predicting their scientific importance across several fields. Despite methodological problems, it is nonetheless widely used to evaluate the academic effect of accomplishments across many disciplines intuitively.[7]

Researchers utilize bibliometric analysis for several purposes, such as cooperation patterns, and research elements, revealing new trends in article, and journal performance, and exploring the intellectual structure of an area of study in the existing literature.[8]

Bibliometric studies aim to objectively examine large data using statistical or graphical approaches, while systematic literature reviews are used to subjectively investigate smaller data [8]. A bibliometric analysis can provide a thorough understanding of a research field and its limits, as well as help identify future research directions. Despite being discussed as early as the 1950s and 1960s, the bibliometric method has become increasingly popular in recent years.[9]

Bibliometric analysis gathers and evaluates data from existing publications, typically sourced from a database, to evaluate current research performance. This approach can enhance our comprehension of the SREBP's role and offer a summary and further evaluation of present research results.

Despite the abundance of studies on SREBP, there is a notable absence of comprehensive bibliometric analyses that systematically examine the annual publication outputs, contributing countries, institutions, journals, authors, keywords, and citation patterns. This gap in the literature makes it difficult for researchers to efficiently navigate the existing body of work, identify key contributors, and determine emerging trends and influential publications within the field.

Our study fills this gap by providing a detailed bibliometric analysis of SREBP research. We offer a comprehensive overview of the research landscape by using tools such as VOSviewer, R version 4.3.2, Biblioshiny, and Excel. This includes identifying prolific countries, institutions, and authors, mapping collaborative networks, and highlighting influential journals and key research themes. Our analysis serves

as a valuable resource for researchers, helping them to select appropriate journals, identify potential collaborators, and align their research with current trends and significant findings in the field of SREBP.

The main objective of our study is to provide a thorough bibliometric analysis of SREBP-related research. By mapping the landscape of this research area, we aim to assess the scientific impact and trends over time, identify key contributors and collaborative networks, and highlight influential publications and emerging topics. We aim to offer strategic insights that guide future research directions, aiding researchers in making informed decisions regarding their studies on SREBP and its diverse biological roles.

Materials and Methods

Despite the fact that there are several bibliometric databases accessible, we choose to use only one. This is because each database has a unique format for bibliometric data collection. Different databases use different formats, which can easily lead to problems [8].

We used the Web of Science (WoS), a widely recognized and high-quality database frequently used in scientometric assessments. As a result, the WoS Core Collection (WoSCC) database was used solely for this inquiry. The first article in WoS, published in 1997, was found through a search of relevant keywords. The bibliometric analysis focused on papers published between 1997 and 2024. The analysis period was selected based on the earliest indexed article (1997) and the most recent available data (2024).

Title, abstract and author keyword searches were conducted using the following search string:

(SREBP *OR* SREBPs *OR* "Sterol element binding protein" *OR* "Sterol element-binding protein") *AND* ("Lipid metabolism" *OR* Lipogenesis)

To focus on original research articles, we excluded document types such as Early Access, Review Articles, Editorial Material, Proceeding Papers, Meeting Abstracts, Book Chapters, Letters, Data Papers, Retracted Publications, Reprints, Corrections, and Retraction materials. After applying these criteria, the initial search yielded 3,963 articles, of which 100 were excluded for not meeting the inclusion criteria. Consequently, 3,863 articles were included in the final analysis.

Information from the WoS database was obtained, including abstract, number of citations, source, the article title, references cited, keywords, WoS categories, publisher information, study areas and author information (names, connections). This data was mapped using the VOSviever application. The search was concluded on January 12, 2024.

VOSviewer, which is widely used in bibliometric research, shows networks between researchers, publications or journals. It also supports co-authorship, citation and bibliometric merging. [10]. Due to these advantages, VOSviewer (version 1.6.18) was used in our research.

In addition to VOSviewer, we used the open source program package The R studio (Version 4.3.2) developed by Aria and Cuccurullo[11]. To analyze the data, we utilized Biblioshiny, a powerful tool in R-Studio's Bibliometrix package. Biblioshiny specializes in visualizing and analyzing bibliometric data. We chose Bibliometrix and Biblioshiny because they offer a wide range of analysis types and modes.[9] In addition, Microsoft Excell 365 application was used for basic statistics and graphics.

This study did not require ethical approval because the data was taken from a public source and there were no human participants.

Results

In the Web of Science database, it was determined that the studies on SREBP were conducted between 1997 and 2024. ***Table 1*** shows an overview of the main criteria of the identified publications. A total of 840 resource types were found, including 3863 documents. The studies obtained were conducted by 13910 authors, citing a total of 103515 references. There was an average of 38.16 citations per article. In total, 6478 different author keywords were used.

Table 1. Information About Data

Timespan	1997:2024
Sources (Journals, Books, etc)	846
Documents	3863
Average citations per doc	38.16
References	103515
Keywords Plus (ID)	6592
Author's Keywords (DE)	6478
Authors	13910
Single-authored docs	29
Co-Authors per Doc	7.08
International co-authorships	%20,76

Keyword plus, one of the methods of analyzing a document, is the keywords found in the reference words of the article.[12] In our sample, 6592 different keyword plus words were identified.

As a result of our research, a total of 27345 authors related to the subject were identified, among which 13910 different researchers wrote 3863 articles.

When the distribution of articles in different categories in the WoS database was analyzed, we encountered 91 different categories, of which biochemistry molecular biology was the field with the highest number of publications when the top ten categories were evaluated.

When we look at the disciplines in which the articles are included, it is an expected result that the fields such as biochemistry, molecular biology, pharmacology and medicine are predominant. (***Figure 1***)

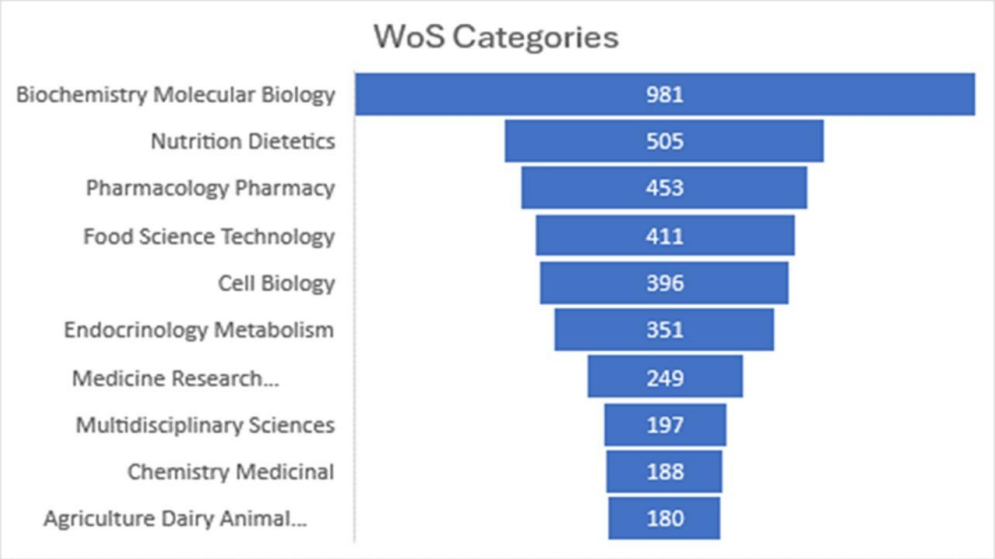

Figure 1. WoS categories in different Diciplines

Figure 2 shows the number of studies conducted each year. The first studies started in 1997 with one article and one paper. The most publications were made in 2022 (n=343).

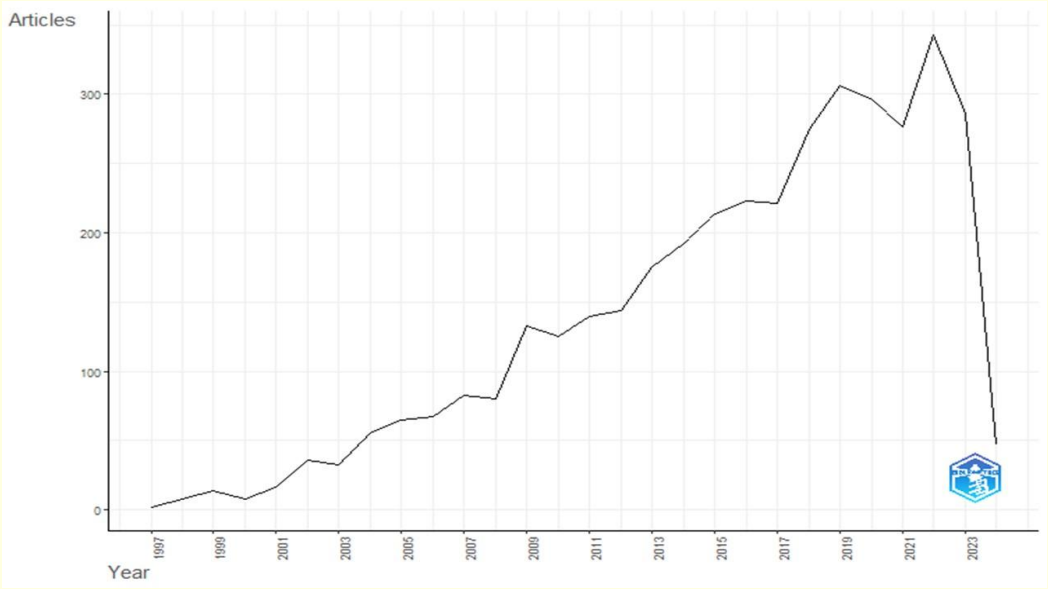

Figure 2. Annual Scientific Production

When the authors involved in the studies included in the research are examined, the authors who published the most in terms of the number of publications were Li X (n=145), Zhang Y (n=133), Li Y (n=126), Wang Y (n=115), Li J (n=98), respectively.

In addition to the keywords used in the studies, we used a Three-Field Plot (Sankey Plot) that shows the words frequently used in the titles by authors working on this topic in the field (***Figure 3***). Thicker rectangles in the diagram represent a higher frequency. The thickness and quantity of connecting nodes, inputs, and outputs imply a higher number of connections. The writers regularly utilized the keywords "lipid metabolism" and "lipid" in their titles, with Zhang Y having the most papers in the field including these phrases.

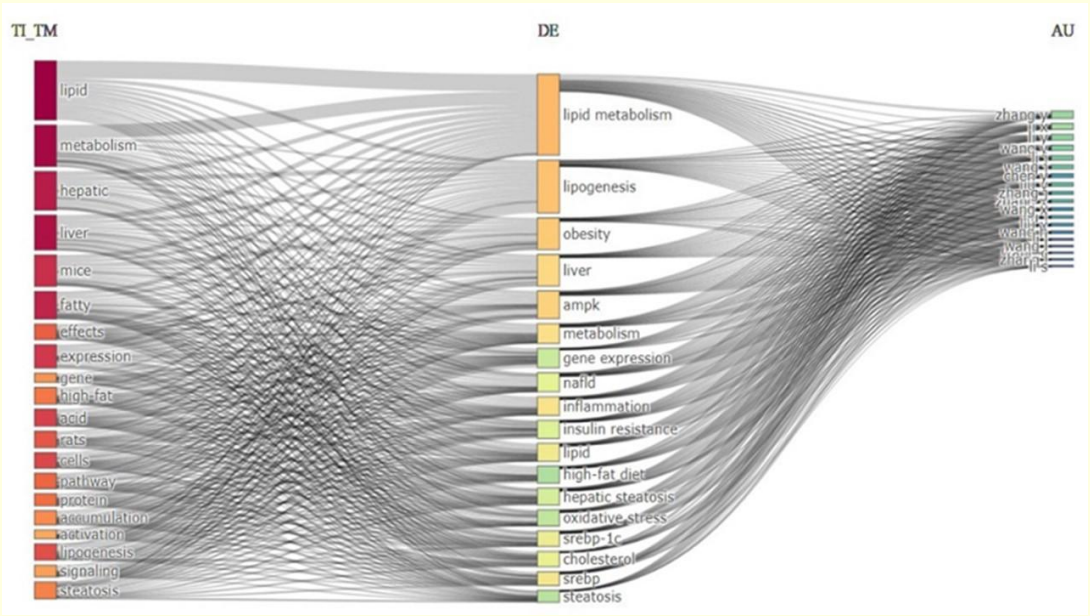

Figure 3. Three-Field Plot

Figure 4 presents a visualized network of keywords with a frequency higher than five, generated using VOSviewer software. The network is divided into fourteen color-coded clusters, each representing a distinct

research theme. The largest cluster, shown in red, includes keywords such as *lipogenesis*, *SREBP*, and *SREBP1*, indicating a focus on lipid metabolism and fatty acid synthesis. The second-largest cluster, colored green, contains terms like *SREBP2*, *cholesterol*, and *atherosclerosis*, reflecting research on cholesterol metabolism. Additionally, other clusters—such as the blue one—highlight disease-related studies, particularly in areas like cancer biology. This color-coded mapping effectively illustrates the thematic structure and diversity within SREBP-related research.

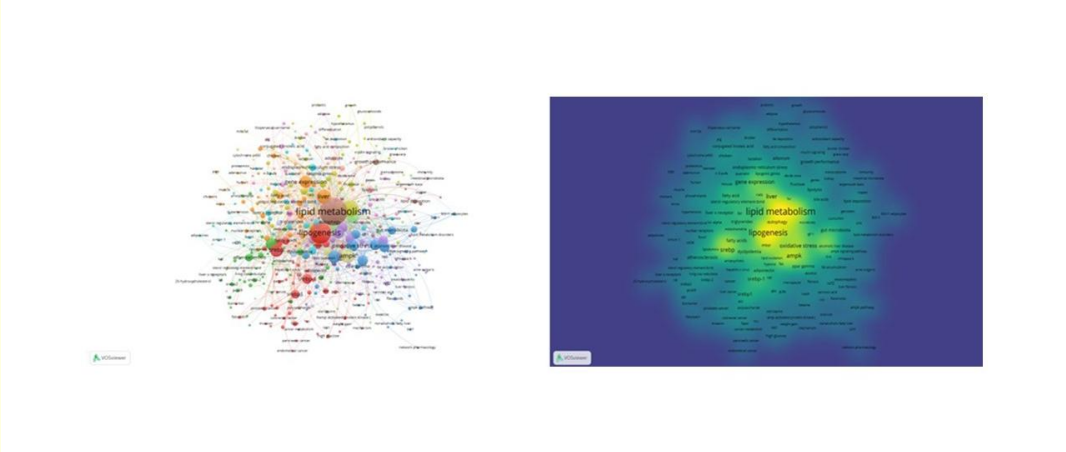

Figure 4 . Network of keywords.

The citation analysis shows a fluctuating but generally increasing trend in the average number of citations per article over the years. The peak was observed in the year 2000 with an average of 343.62 citations per article. This indicates that certain landmark studies published during these years have had a significant impact on the field.

The h-index is a metric at the author level that assesses both the productivity and citation impact of a scientist or academic's publications. The g-index places greater emphasis on highly cited articles. The m-index is the ratio of an author's h-index to the number of years since their first publication, though it is not commonly used. [13] When examining the index evaluation of the journals with the highest publication numbers, the top 5 journals ranked by h-index are listed in the ***Table 2***. The h-index, g-index, and m-index provide insight into the citation impact and productivity of journals in SREBP research.

Table 2. Top 5 journals ranked by h-index, g index, m-index

Journal	h_index	g_index	m_index	TC	NP	PY_start
JOURNAL OF BIOLOGICAL CHEMISTRY	59	109	2,10714286	12255	109	1997
JOURNAL OF LIPID RESEARCH	39	67	1,625	4593	72	2001
DIABETES	32	37	1,39130435	4950	37	2002
HEPATOLOGY	31	37	1,40909091	2851	37	2003
PLOS ONE	31	49	1,9375	2827	78	2009
JOURNAL OF NUTRITIONAL BIOCHEMISTRY	30	43	1,42857143	1955	52	2004
JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY	26	42	1,52941176	1883	58	2008
AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM	25	34	0,96153846	2616	34	1999
FOOD \& FUNCTION	24	39	1,84615385	1626	53	2012
BRITISH JOURNAL OF NUTRITION	23	37	1,0952381	1397	40	2004

TC:total citiations, NP: number of product PY:product year.

China ranks first in the scientific production of all countries with 7042 publications. This is followed by USA (n=2869), South Korea (n=2021), Japan (n=1113), Germany (n=428). Studies on SREBP started with 1 article published in the United States of America in 1997 and only 14 articles were published in the following year.. In Turkey, 61 publications were written on the subject. (***Figure 5***)

Figure. 5 A. Country production **B.** Corresponding author's (Single Country Publication (SCP) and Multiple Country Publication (MCP) numbers) **C.** Most cited countries **D.** Country scientific production

Although it is not the first in the ranking of the country with the most publications, USA ranks first in the ranking of the country with the most citations. It received 51554 citations in total, which is 35.11% of the total number of citations among all countries. The United States was followed by China, Japan, Korea, France. It's also worth noting that having a lot of articles doesn't always mean having a lot of citations. Finland is first in terms of the mean amount of citations per manuscript, followed by the United States, France, the United Kingdom, and Ireland.

A comparison between the number of articles and the number of citations reveals that a high volume of publications does not automatically result in a high number of citations (***Figure 5***). When responsible authors are analyzed, China, the USA and Korea rank in the top three in both Single Country Publication (SCP) and Multiple Country Publication (MCP) numbers (***Figure 5***).

When we analyze the affiliated institutions, Seoul National University is followed by Najing Agr University and China Pharmaceutical University. There are also eight articles from Mersin University from Turkey. (***Table 3***)

Table 3. Affiliated institutions

Affiliation	Articles
SEOUL NATL UNIV	183
NANJING AGR UNIV	143
CHINA PHARMACEUT UNIV	123
SUN YAT SEN UNIV	117
KYUNG HEE UNIV	113

JILIN UNIV	107
UNIV TOKYO	106
FUDAN UNIV	105
HUAZHONG AGR UNIV	104
CHONGQING MED UNIV	103

Discussion

The extended role of SREBPs beyond lipid metabolism, encompassing endoplasmic reticulum (ER) stress, inflammation, autophagy, and apoptosis, underscores their versatility in cellular regulation .[14] The high citation rates of studies focusing on these areas indicate a growing interest in the broader implications of SREBP in pathophysiological conditions.[15] For instance, the link between SREBP activity and metabolic diseases such as obesity, diabetes, and cardiovascular diseases has been well-documented . Additionally, emerging evidence suggests that SREBPs are involved in cancer biology, influencing tumor growth and survival through lipid metabolism reprogramming.[16]

Tumor cells often exhibit altered lipid metabolism to support rapid cell proliferation and survival. SREBPs, particularly SREBP-1, are upregulated in various cancers and are involved in the synthesis of lipids required for membrane biogenesis and signaling molecules. Inhibiting SREBP activity in cancer cells has been shown to reduce tumor growth and enhance the efficacy of chemotherapeutic agents. This highlights the potential of SREBPs as therapeutic targets in oncology.[17]

Bibliometric analysis is widely used to evaluate trends and development in a variety of scientific domains. Currently, there is no bibliometric analysis of SREBP. This research employs bibliometric analysis to thoroughly examine the current state and development trends of SREBP from 1997 to 2024.

Our analysis indicates that the United States, China, and South Korea are leading in terms of the number of publications and citations related to SREBP research. This dominance likely results from high biomedical investment, strong infrastructure, and active collaborations in these countries. Specifically, Seoul National University, Nanjing Agricultural University, and China Pharmaceutical University have emerged as prominent institutions, demonstrating significant contributions to the field. These institutions have focused on various aspects of SREBP, ranging from its basic biological functions to its roles in disease mechanisms, reflecting the multifaceted nature of SREBP research.

In our research, we encountered 91 different categories. Articles are categorized according to the place of publication. In the diagram given in the results, a publication can be associated with more than one category. Therefore, the number of documents in category groups is higher than the total number of documents.

The geographic distribution of research output shows a notable concentration in Asia, particularly in China and South Korea. This trend is reflected in the collaborative networks visualized through VOSviewer, where institutions in these countries form dense clusters, indicating robust national and international collaborations. The predominance of these collaborations suggests that future research may benefit from leveraging these networks to enhance cross-border studies and share technological advancements.

In contrast, while the United States has fewer publications compared to China, it leads in total citations, indicating a higher impact of its research. This discrepancy highlights the quality and influence of research emerging from U.S. institutions, which often set foundational theories and methodologies in the field. The high average citations per paper in countries like the USA and Finland suggest that these regions are producing highly influential research that shapes subsequent studies globally. Similarly, Finland has the

highest average number of citations per article, indicating that this country has conducted few but effective studies.

Bartel D. P., Esau C., and Zhang Y., who are among the most cited authors, stand out as researchers who have made significant contributions in this field. Especially Zhang Y.'s being the most published author and being associated with frequently used keywords emphasizes the central role of this author in the field of SREBP. The results show that only 29 documents are single-authored papers, indicating that the high complexity of the topic requires collaboration with other researchers. This is evidenced by the fact that, on average, about five researchers contributed to a single paper.

In addition, this study has certain limitations. Our study only examined articles from the Web of Science (WoS) database and did not include studies from other databases. The use of different databases may provide a broader and different perspective. Furthermore, the fact that we only analyzed original research articles may have led us to ignore contributions from review articles and other document types.

Given the comprehensive dataset spanning over two decades, several future research directions can be proposed:

1. Interdisciplinary Studies: The intersection of SREBP research with other biological processes such as autophagy, inflammation, and apoptosis opens new avenues for interdisciplinary studies. Investigating these intersections can provide a holistic understanding of how lipid metabolism interacts with other cellular functions in health and disease.

2. Therapeutic Targeting: The role of SREBPs in metabolic diseases and cancer highlights their potential as therapeutic targets. Future research should focus on developing and testing SREBP inhibitors or modulators in clinical settings, assessing their efficacy and safety in treating these conditions.

3. Technological Innovations: Advancements in technologies such as CRISPR/Cas9 for gene editing and single-cell RNA sequencing can be leveraged to study the specific functions of SREBP isoforms in various tissues . These technologies can help elucidate the precise regulatory mechanisms of SREBPs and their impact on cellular metabolism.

4. Global Collaborative Efforts: Encouraging international collaborations, particularly involving underrepresented regions in current SREBP research, can enhance the diversity and scope of studies. Collaborative efforts can facilitate the sharing of resources, expertise, and data, fostering a more inclusive and comprehensive research environment.

In addition, strengthening international collaborations in SREBP research can accelerate discoveries in lipid metabolism and disease mechanisms and enable translational applications.

Conclusion

The bibliometric analysis provides a detailed overview of the research trends and contributions in the field of SREBP. The findings underscore the significance of SREBPs in lipid metabolism and beyond, with implications for various diseases. By identifying key contributors, collaborative networks, and emerging research areas, this study offers valuable insights for future research directions, aiming to enhance our understanding of SREBPs and their potential therapeutic applications.

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Author Contributions

Şerife Efsun Antmen: Idea/concept, design, supervision, data collection and processing, interpretation, literature review, writing the article, critical review.

Cem Yalaza: Idea/concept, design, supervision, data collection and processing, interpretation, literature review, writing the article, critical review.

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