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Systematic Review

A Bibliometric Analysis of Publications on Ferritinophagy from 2014 to 2021

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Abstract

Objective: This study was to explore the research status and research hotspots of ferritinophagy in the past eight years. **Methods**: Relevant papers on ferritinophagy from 2014 to 2021 was retrieved from the science citation extended database of the Web of Science. Through the application of bibliometrics research methods and bibliometrics analysis software VOSviewer to extract, analyze and visualize journals, authors, research institutions and keywords, to clarify the hot spots and development history of peritoneal dialysis research. **Results**: A total of 134 studies were screened and included in this study. Overall, the output of ferritinophagy research had fluctuated in the past 8 years. China's research on ferritinophagy had the largest number of published articles. The United States still maintained a leading position in research in this field, and its citation frequency, H-index and funding output are all at the forefront. Among them, international cooperation with relevant institutions was also more frequent. Ferritinophagy was currently mainly focused on cell biology. Tumor research might be the next major clinical research direction in this field. The related research on oxidative stress pathways, cell death methods, and nuclear receptor co-activator 4 (NCOA4) in the field of ferritinophagy were current research hotspots. **Conclusions**: It could be understanding the research status and hotspots of ferritinophagy in the world more clearly and intuitively by using the bibliometric method.

Keywords: ferritinophagy; bibliometrics; visual analysis; VOSviewer

1.Introduction

Iron is an element essential for cell proliferation and growth, and it is also an important cofactor for metabolic enzymes, closely related to many biological processes such as neurotransmitter transmission, oxygen transport, cell division, and energy generation [1]. Iron is divided into two reversible compound states of reduced Fe^{2+} and oxidized Fe^{3+}. Changes in iron content are closely related to cell function, and insufficient content can lead to electron transport and energy metabolism disorders, developmental defects, and hemoglobin deficiency. On the contrary, iron overload can produce reactive oxygen species (ROS) through Fenton reaction to mediate oxidative stress, destroy DNA, protein and lipids, and participate in the occurrence and development of chronic cirrhosis, diabetes, heart failure, arthritis and neurodegenerative diseases [2]. The body needs to maintain cellular and internal iron homeostasis to meet the physiological requirements of metabolism and prevent iron overload caused by excessive accumulation [3].

Ferritinophagy was firstly proposed that was a selective autophagy that regulated iron content in cells by specifically mediating the movement of ferritin to lysosomes and degrading and releasing free iron [4]. Nuclear receptor coactivator 4 (NCOA4) is considered to be a key regulator of iron autophagy, which targets to ferritin and is transferred to lysosome for degradation and release of free iron. Iron autophagy mediated by NCOA4 constitutes an important part of iron metabolism [5,6]. Therefore, understanding how iron autophagy leads to ferritinophagy in a variety of pathological environments in vivo, and in-depth study of the role of NCOA4 in anemia, neurodegenerative diseases, cancer and related diseases such as ischemia/reperfusion injury will be key to the development of therapeutic interventions. However, the current research status and focus of ferritinophagy are still unknown.

Ferritinophagy has been widely concerned at home and abroad, and the number of studies is increasing year by year. To analyze the research status and development trend of ferritinophagy is helpful to understand the research status and promote the development of iron autophagy. As early as the beginning of the 20th century, people began to conduct quantitative research on literature, but bibliometrics did not exist as an independent discipline at that time. It was not until 1969 that Alan Pritchard, a famous British intelligence scientist, first proposed to replace the term "bibliography" with the term "Bibliometrics". The emergence of this term marks the formal birth of bibliometrics. Bibliometrics is a quantitative and qualitative study of the history, current situation and development law of a certain field of literature based on the literature itself, and its research results can provide reference for the formulation of guidelines and related personnel to conduct research in this field [7].

At present, bibliometrics and visual analysis have been applied in many disciplines such as anesthesiology, ophthalmology, stomatology and obstetrics and gynecology [8–11], but there are no bibliometrics articles about ferritinophagy. Visualization of Similarities Viewer (VOSviewer1.6.17, Leiden University, Leiden, The Netherlands) is a web software tool for building and visualizing bibliometrics, launched by Ness Jan van Eck and Dr. Ludo Waltman of Erasmus University in the Netherlands in 2009. The software can analyze the authors, keywords, and units in the literature, and can more accurately grasp the hotspots of a certain research field [12]. At present, VOSviewer is one of the frequently used software in the field of library and information. From the design goal of the VOSviewer software itself, there is no obvious subject attribute, it can help researchers in different disciplines to visually analyze the literature in their fields. As a software for constructing and visualizing bibliometric networks, VOSviewer is being favored by more and more researchers because of its features such as free access, rich functions, convenient and efficient bibliographic data processing, and good visualization effects. And VOSviewer can provide a total of 4 views: label view, density view, cluster density view and scatter view, which create good conditions for data visualization.

The bibliometric analysis has been used to in the hot topic "ferroptosis in Stroke" From 2013 to 2021 [13]. Based on the reported study, Web of Science database, literature metrology and visual analysis were conducted on retrieved papers on ferritinophagy. This paper discussed the development process, research status and future trend of ferritinophagy, aiming to provide reference for further research in ferritinophagy.

2. Methods

2.1 Bibliometric Data

This study adopted the same approach as previous similar literature [14]. PubMed and Web of Science databases were used for searching. All data were obtained on March 12, 2022. Since these data were downloaded from a public database, there are no ethical concerns, so we did not make an ethical application. Retrieved by the subject heading "ferritinophagy", the time was set from 2014 to 2021. This study obtained full records of literature, including title, year of publication, author, country (region), research institution, journal name, keywords, funding and abstract. Conference abstracts, editorials, letters, news reports, summaries were excluded. The impact factor was taken from the 2021 Journal Citation Reports database.

2.2 Search Strategy

The search terms in WOS were as follows: TOPIC: (ferritinophagy) Refined by: DOCUMENT TYPES: (ARTICLE OR PROCEEDINGS PAPER OR REVIEW OR MEETING ABSTRACT) AND LANGUAGES: (ENGLISH) Indexes = SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED. In PubMed, the search terms were as follows: "ferritinophagy"[MeSH Terms] OR "ferritinophagy"[All Fields]) AND English [lang].

2.3 Bibliometric Analysis

The number and quality of pares related to ferritinophagy from 2014 to 2021 were sorted out by the literature statistics tool that comes with the Web of Science database. The top 10 most cited articles were also listed. In this study, the visualization tools VOSviewer and Microsoft Excel were used to extract and process information such as publication year, journal, country, author, funding, and institution of the retrieved literature.

3. Results

3.1 Global Research Status of Ferritinophagy

As shown in Fig. 1A, after database search and inclusion and exclusion criteria screening, from 2014 to 2021, this study retrieved 134 and 146 valid literatures from WOS and PubMed databases, respectively. Due to differences in the content of journals included in the two databases, the results might not be exactly the same. As shown in Fig. 1B, there had been an upward trend in the number of publications related to ferritinophagy in the world between 2014 and 2021, reflecting the growing interest in ferritinophagy research over the past 8 years. As shown in Fig. 1C, our findings showed that 21 countries worldwide had been involved in ferritinophagy research. Among them, China (75 articles, 55.97%) published the largest number of articles in this field, USA (47 articles, 35.07%) ranked second, Italy (9 articles, 6.72%), France (7 articles, 4.76%) and Japan (7 articles, 4.76%) ranked 3rd, 4th and 5th. Among the top five countries with the largest number of publications, China had the largest increase.

As shown in Fig. 1D, using the keyword co-occurrence analysis of VOSviewer software, the articles cooperated with each other more than once as the inclusion criteria. The analysis showed that 21 countries published more than 1 paper. It includes five countries (regions) for cooperation: Australia, Canada, the United Kingdom, Finland, Japan, the Philippines and Saudi Arabia cooperation network, France, Italy and Sweden cooperation network, Iran, Poland and the United States cooperation network, Belgium and Germany cooperation network, China-Singapore cooperation network (Fig. 1D). Therefore, transnational and transregional exchanges in the field of ferritinophagy were very common.

3.2 Analysis of Citations, H-Index and Cooperation Status of Papers Published by Various Institutions

As shown in Fig. 2A, from the perspective of the number of published papers, it was found that Harvard University, Dana Farber Cancer Institute, Harvard Medical

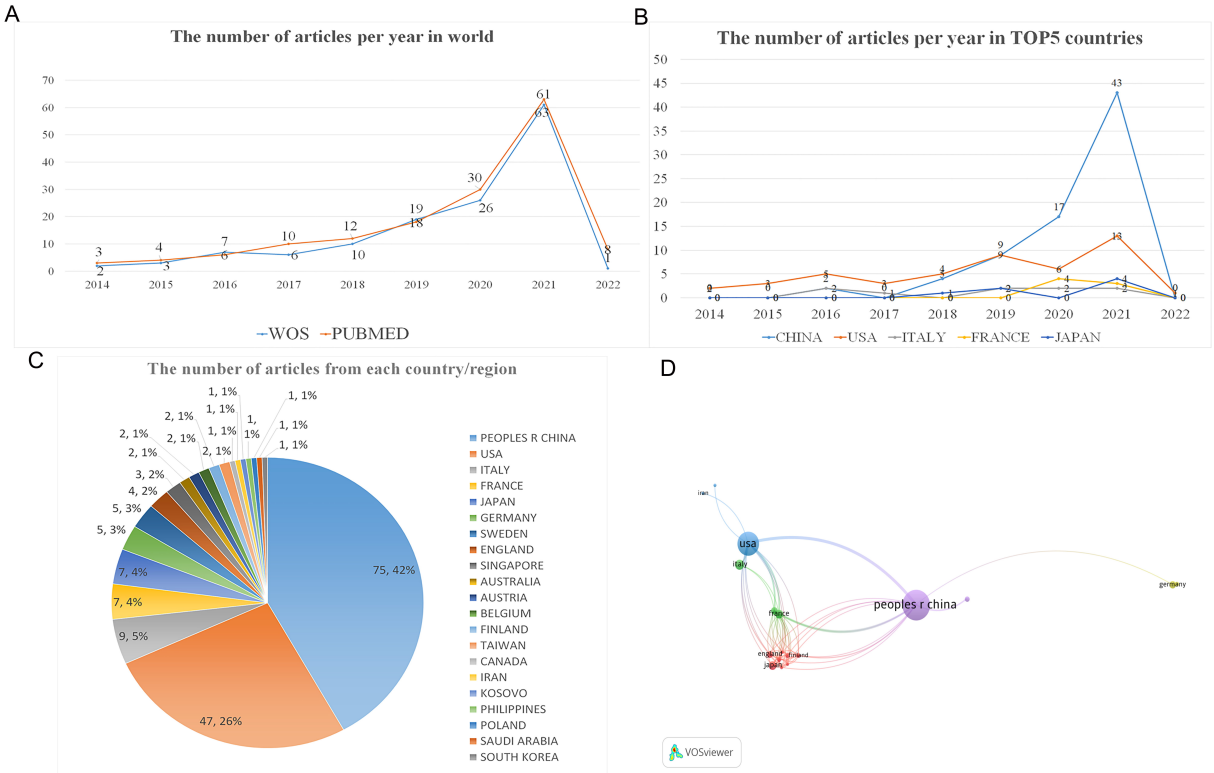

Fig. 1. Global research status of ferritinophagy. (A) From 2014 to 2021, this study retrieved 134 and 146 valid literatures from WOS and PubMed databases, respectively. (B) There had been an upward trend in the number of publications related to ferritinophagy in the world between 2014 and 2021. (C) 21 countries worldwide had been involved in ferritinophagy research. Among them, China (75 articles, 55.97%) published the largest number of articles in this field, USA (47 articles, 35.07%) ranked second, Italy (9 articles, 6.72%), France (7 articles, 4.76%) and Japan (7 articles, 4.76%) ranked 3rd, 4th and 5th. Among the top five countries with the largest number of publications, China had the largest increase. (D) There were close cooperation relationships between countries, and the cooperation network covers all countries (regions). Our analysis revealed that only 21 countries published more than 1 paper, while 5 were closely related. Among them, Australia, Australia, Canada, England, Finland, Japan, Philippibes and Saudi Arabia were closely linked. The three countries France, Italy and Sweden were closely linked. There were strong linked between Iran, Poland and USA. Belgium and Germany are closely linked. There was a close correlation between China and Singapore.

School, Shanghai JiaoTong University and University of Texas Southwestern Medical Center Dallas had published the most papers on Top 5 institutions with the most literature on autophagy. As shown in Fig. 2B, Harvard University had the highest number of published articles (7), total citations (1072), and H-index (8) in the world. Articles published by Dana Farber Cancer Institute had the highest number of citations per article (145.57).

As shown in Table 1 (Ref. [2,4,15–22]), the article published by Harvard University, "Quantitative proteomics identifies NCOA4 as the cargo receptor mediating ferritinophagy", written by Mancias, Joseph D, and co-authors published in the journal "NATURE" in 2014, was cited the most times (615) [15]. In this study, ferritinophagy was first proposed, and nuclear receptor coactivator 4 (NCOA4) was identified by quantitative proteomics as a selective autophagy receptor that mediates ferritin in autophagosomes was degraded, so that iron ions bound to ferritin were released as free iron, and this process was called ferritinophagy. Under normal physiological conditions, iron was stored in ferritin, but when intracellular iron was deficient, ferritin containing iron ions binds to NCOA4 to form a complex, which mediates autophagy to release iron ions. NCOA4 was confirmed to be a protein with a molecular mass of 70 kDa by quantitative proteomic methods. NCOA4 included four domains, namely NCOA4α, NCOA4β, NCOA4-N-terminal and NCOA4-C-terminal [15].

In order to further analyze the relationship between the institutions that published ferritinophagy literature, we used VOSviewer software to include more than or equal to 1 article as the inclusion criterion, and included all institutions in the analysis. As shown in Fig. 2C, Guangzhou Med Uni, Hop Europeen Georges Pompidou, Univ Michigan, Univ Paris, ut Southwestern Med Ctr cooperate closely. Cen South Univ and Huazhong Univ Sci & technol cooperate closely. Dana Farber Cancer Institute and Harvard Medical School work closely together.

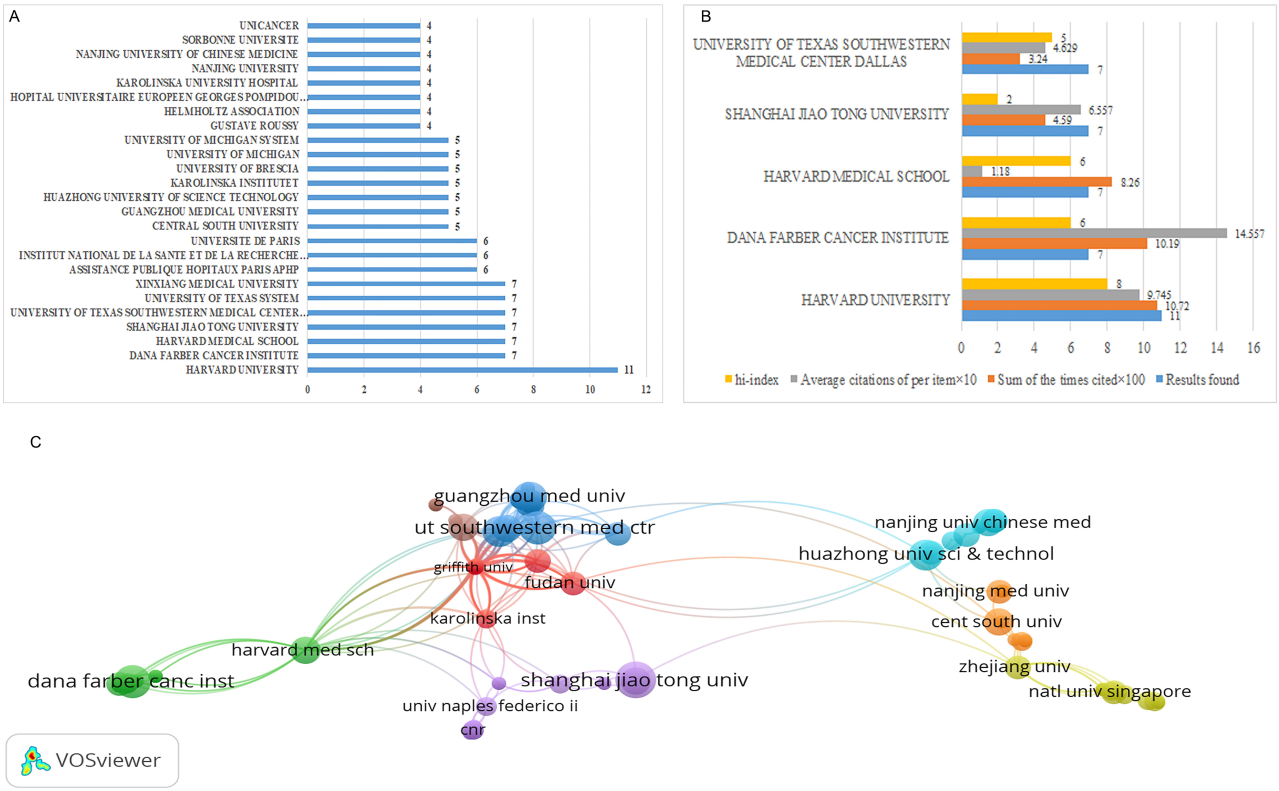

Fig. 2. Analysis of citations, H-index and cooperation status of papers published by various institutions. (A) Harvard University, Dana Farber Cancer Institute, Harvard Medical School, Shanghai JiaoTong University and University of Texas Southwestern Medical Center Dallas had published the most papers on Top 5 institutions with the most literature on autophagy. (B) Harvard University had the highest number of published articles (7), total citations (1072), and H-index (8) in the world. Articles published by Dana Farber Cancer Institute have the highest number of citations per article (145.57). (C) Guangzhou Med Uni, Hop Europeen Georges Pompidou, Univ Michigan, Univ Paris, ut Southwestern Med Ctr cooperate closely. Cen South Univ and Huazhong Univ Sci & technol cooperate closely. Dana Farber Cancer Institute and Harvard Medical School work closely together.

3.3 Analysis of Main Funding Funds Supporting Ferritinophagy Research

As shown in Fig. 3, the funding analysis results showed that a total of 200 funds participated in the funding. The National Natural Science Foundation of China (NSFC) supported the production of the largest number of papers, supporting the publication of 60 papers, each accounting for 44.78% of the total number of publications in the world. Second, the National Institutes of Health NIH USA and the United States Department of Health Human Services both supported the output of 28 papers, accounting for 20.90%. The number of literatures supported by NIH National Cancer Institute NCI ranks fourth in the world, with a total of 12 literatures published, accounting for 8.96%.

3.4 Analysis of Published Journals and Subject Words

As shown in Fig. 4A, a total of 102 different journals around the world had published research results related to ferritinophagy. Among them, OXIDATIVE MEDICINE AND CELLULAR LONGEVITY, AUTOPHAGY, BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, FREE RADICAL BIOLOGY AND MEDICINE, JOURNAL OF CELLULAR PHYSIOLOGY ranked the top five, and published 6, 5, 5, 5, and 4 articles respectively. Our research on ferritinophagy "Inhibition of DNMT-1 alleviatings ferroptosis through NCOA4 mediated ferritinophagy during diabetes myocardial ischemia/reperfusion injury" was published in CELL DEATH DISCOVERY [23]. The journal published 3 papers related to ferritinophagy.

As shown in Fig. 4B, by analyzing the subject words of ferritinophagy related literature, it was found that the top ten occurrences of the subject words are Cell Biology (38 times), Biochemistry Molecular Biology (37 times), Pharmacology Pharmacy (13 times), Oncology (10 times), Biophysics (8 times), Medicine Research Experimental (8 times), Toxicology (8 times), Endocrinology Metabolism (7), Hematology (7), Chemistry Multidisciplinary (6).

3.5 Keyword Analysis in Ferritinophagy Related Literature

By using VOSviewer software, it was found that there were 659 keywords in all ferritinophagy related literatures.

Table 1. The top 10 most cited articles on ferritinophagy research in the world.

Title	Authors	Total citations	Average per year	Source title	Publication date
Quantitative proteomics identifies NCOA4 as the cargo receptor mediating ferritinophagy	Mancias, Joseph D. *et al.* [15]	591	65.67	NATURE	MAY 1 2014
Autophagy at the crossroads of catabolism and anabolism	Kaur, Jasvinder. *et al.* [16]	550	68.75	NATURE REVIEWS MOLECULAR CELL BIOLOGY	AUG 2015
Autophagy promotes ferroptosis by degradation of ferritin	Hou, Wen. *et al.* [2]	517	73.86	AUTOPHAGY	2016
Ferroptosis is an autophagic cell death process	Gao, Minghui. *et al.* [17]	440	62.86	CELL RESEARCH	SEP 2016
Ferroptosis: Role of lipid peroxidation, iron and ferritinophagy	Latunde-Dada, Gladys O. *et al.* [18]	225	37.5	BIOCHIMICA ET BIOPHYSICA ACTA-GENERAL SUBJECTS	AUG 2017
Iron and cancer: recent insights	Manz, David H. *et al.* [19]	187	26.71	COOLEY'S ANEMIA	2016
Role of GPX4 in ferroptosis and its pharmacological implication	Seibt, Tobias M. *et al.* [20]	175	43.75	FREE RADICAL BIOLOGY AND MEDICINE	MAR 2019
Ferritinophagy via NCOA4 is required for erythropoiesis and is regulated by iron dependent HERC2-mediated proteolysis	Mancias, Joseph D. *et al.* [4]	170	21.25	ELIFE	OCT 5 2015
The Hallmarks of Ferroptosis	Dixon, Scott J. *et al.* [21]	155	38.75	ANNUAL REVIEW OF CANCER BIOLOGY, VOL 3	2019
Ferroptosis is a type of autophagy-dependent cell death	Zhou, Borong. *et al.* [22]	152	50.67	SEMINARS IN CANCER BIOLOGY	NOV 2020

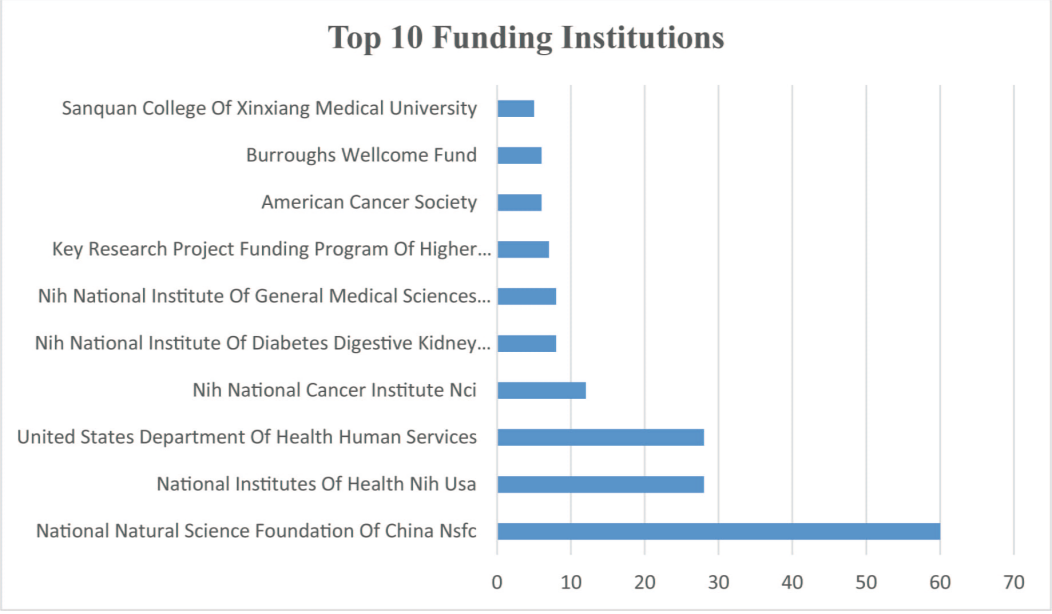

Fig. 3. Analysis of main funding funds supporting ferritinophagy research. A total of 200 funds participated in the funding. The National Natural Science Foundation of China (NSFC) supported the production of the largest number of papers, supporting the publication of 60 papers, each accounting for 44.78% of the total number of publications in the world. Second, the National Institutes of Health NIH USA and the United States Department of Health Human Services both supported the output of 28 papers, accounting for 20.90%. The number of literatures supported by NIH National Cancer Institute NCI ranks fourth in the world, with a total of 12 literatures published, accounting for 8.96%.

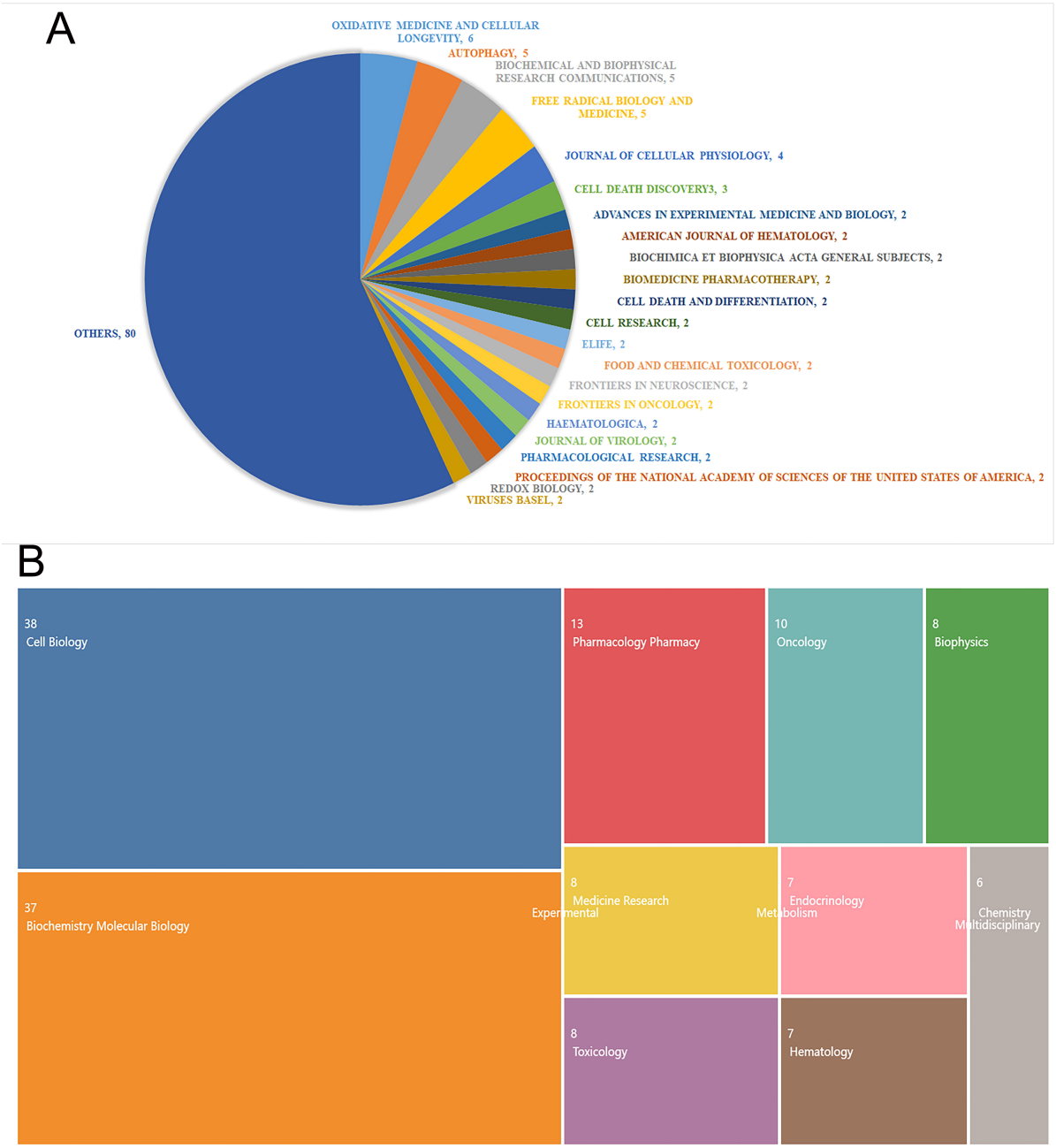

Fig. 4. Analysis of published journals and subject words. (A) A total of 102 different journals around the world had published research results related to ferritinophagy. Among them, OXIDATIVE MEDICINE AND CELLULAR LONGEVITY, AUTOPHAGY, BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, FREE RADICAL BIOLOGY AND MEDICINE, JOURNAL OF CELLULAR PHYSIOLOGY ranked the top five, and published 6, 5, 5, 5, and 4 articles respectively. (B) The top ten occurrences of the subject words are Cell Biology (38 times), Biochemistry Molecular Biology (37 times), Pharmacology Pharmacy (13 times), Oncology (10 times), Biophysics (8 times), Medicine Research Experimental (8 times), Toxicology (8 times), Endocrinology Metabolism (7), Hematology (7), Chemistry Multidisciplinary (6).

The top five keywords with the highest number of occurrences were ferritinophagy (72 times), ferroptosis (65), autophagy (61), iron (48), NCOA4 (29). The corresponding Total link strengths were 335, 319, 301, 231, and 152, respectively. To further analyze the relationship between keywords, when we used VOSviewer software, we took the occurrence of keywords more than or equal to 5 times as the inclusion criteria, and a total of 35 keywords were included in the analysis. As shown in Fig. 5, the relationship between ferritinophagy, ferroptosis, ferritin, degradation, NCOA4, iron homeostasis and metabolism were relatively close. Iron, cell-death, cancer-cells, lipid-peroxidation and

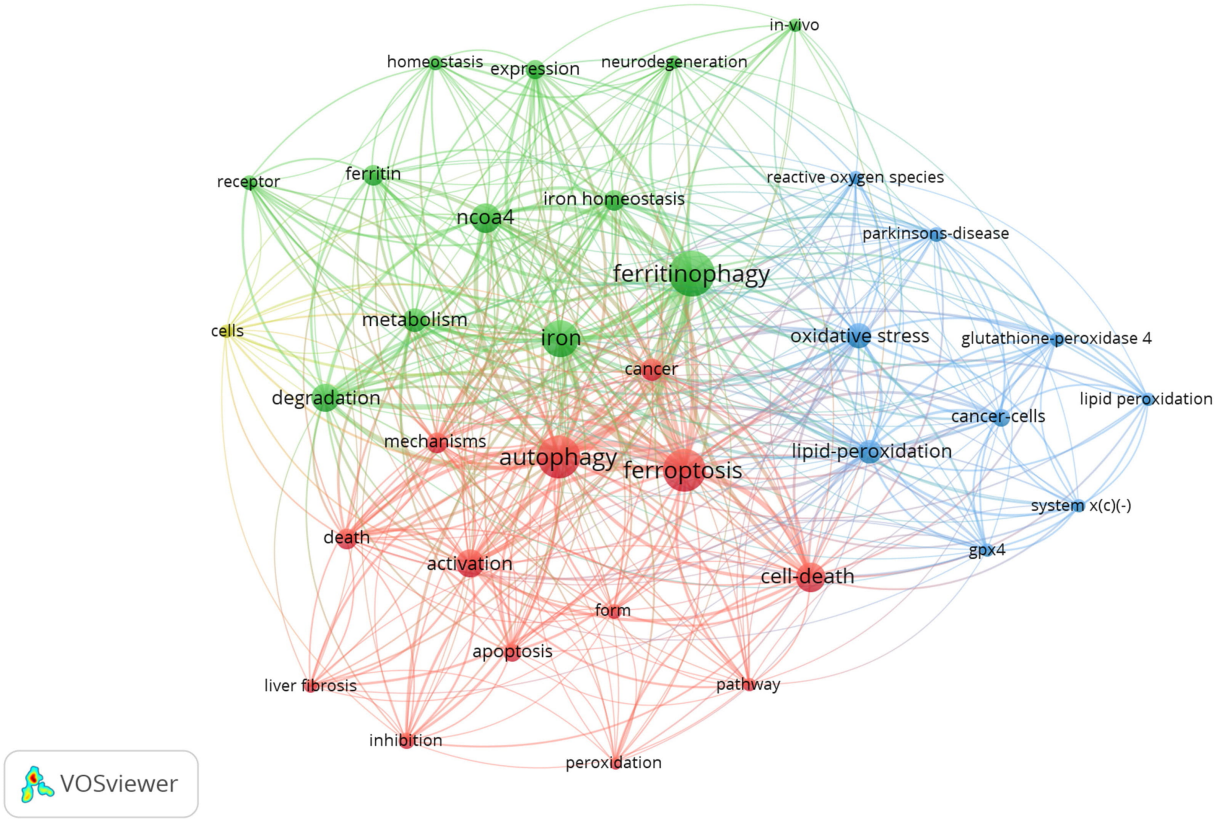

Fig. 5. Keyword analysis in ferritinophagy related papers. The relationship between ferritinophagy, ferroptosis, ferritin, degradation, NCOA4, iron homeostasis and metabolism were relatively close. Iron, cell-death, cancer-cells, lipid-peroxidation and oxidative stress were closely related. Autophagy, apoptosis, activation, cancer, death, inhibition, mechanisms were closely related.

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4. Discussion

Since ferritinophagy was first proposed, the basic and clinical researches related to ferritinophagy have made great progress. H-ferritin binds up to 24 NCOA4 (383-522) fragments to form a highly stable and insoluble complex. This iron-dependent and highly stable "H-ferritin-NCOA4 complex" has important implications for the characterization of ferritinophagy mechanisms [24]. Iron deposition in senescent cells is associated with impaired ferritinophagy function and inhibition of ferroptosis [25]. NCOA4-mediated ferritinophagy can selectively target iron overload diseases without disrupting the physiological processes involved in the response to systemic iron deficiency [26]. Apolipoprotein E effectively inhibits ferroptosis by blocking ferritinophagy, which has important implications for the treatment of Alzheimer's disease (AD) [27]. Moreover, studies have confirmed (embryonic lethal, abnormal vision, drosophila)-like 1 (ELAVL1)/ferritinophagy pathway as a potential target for the treatment of liver fibrosis [28]. Deletion of the NCOA4 gene in mouse hearts reduces left ventricular cavity size and improves cardiac function, and the lipid peroxidation inhibitor ferrostatin-1 attenuates the progression of dilated cardiomyopathy by inhibiting NCOA4-mediated ferritinophagy [29]. Meanwhile, NCOA4-mediated ferritinophagy is a key link in chronic obstructive pulmonary disease (COPD) induced by cigarette smoke (CS) [30].

In this study, the bibliometric visualization software VOSviewer was used to analyze the literature on ferritinophagy in the Web of Science database in the past 8 years. It presented in the form of network tables, visualization and collinear clustering knowledge map. Judging from the year of publication, there were 134 ferritinophagy papers published in international journals from 2014 to 2021, and the number of papers published in the past 8 years had increased year by year, indicating that ferritinophagy had gradually attracted the attention of nursing researchers. Judging from the published journals, the research literature was published in 102 journals, and each journal published an average of 1.314 articles, but there were 80 journals that only published one article, accounting for 78.4%, most of which were basic medicine, biology and comprehensive. Journals, journals of clinical medicine are very few. This suggests that there is an imbalance in the journals ferritinophagy studies, and there are large differences in the number of publications.

From the perspective of the country that issued the article, although China had the largest number of articles, there were 75 articles, accounting for 55.97% of the total amount of articles. The United States followed closely with 47 articles, accounting for 35.07% of the total. However, the total number of citations, the citation rate of a single article and the H-index published by American institutions rank first in the world, which shows that the United States is ahead of other countries in the field of ferritinophagy research in terms of quantity and quality. The quality and quantity of scientific research results are inseparable from the financial support and mutual cooperation provided by funding agencies. In the ranking of funding funds, although American institutions are not the institutions that support the largest number of published articles, the total number of articles funded by funds provided by American institutions accounts for more than half of the total number of articles published, which shows that the United States has invested a lot in the field of ferritinophagy research. In terms of author cooperation, the main authors form 5 cooperative groups, each group is based on a country or region. There is close cooperation within the teams, but little mutual cooperation between teams. It is recommended to strengthen the cooperation between teams. In the future, multi-disciplinary and multi-center cooperative research will become a mainstream trend. The article can be seen in the co-authorship analysis that China and the United States have the highest link strength in countries co-authored, indicating that China and the United States have extensive cooperation with countries around the world. Therefore, the article can see that the United States has absolute advantages in financial support, cooperation, and literature quality. Although China has the highest number of publications on ferritinophagy and the most funding from the National Natural Science Foundation of China (NSFC) in China, the quality of publications in China needs to be improved. It can be seen that the United States is the country with the strongest scientific research strength in the field of ferritinophagy research.

From the perspective of publishing institutions, the top 10 research institutions with published papers were all university research groups, hospitals, and research institutes. In terms of institutional cooperation, 7 clusters were generated among institutions that had published more than one article, and each cluster was roughly divided into regions. This study suggests that with the gradual development of the institutionalization of Ferritinophagy, research institutions should gradually tilt toward clinical hospitals. The clinical transformation of Ferritinophagy research should be strengthened to jointly promote the application of ferritinophagy related research to clinical diseases for the benefit of human health.

Judging from the journals that published the article, there were 102 different journals that have published related research results on ferritinophagy. OXIDATIVE MEDICINE AND CELLULAR LONGEVITY magazine published the most articles with 6. Among them, there are also many top magazines like NATURE, BLOOD, and CELL RESEARCH. Although the number of publications was not large, there was only one article. But as "Quantitative Proteomics identifies NCOA4 as the cargo receptor mediating ferritinophagy" published in NATURE in 2014 [15]. The concept of Ferritinophagy was first proposed. This study was cited as many as 615 times, indicating that all subsequent studies on Ferritinophagy were based on this study.

By analyzing the subject words, it was found that the most frequent subject words were Cell Biology, Biochemistry Molecular Biology, Pharmacology Pharmacy, Oncology, and Biophysics. At the same time, the further keyword analysis was found that ferroptosis, autophagy, iron and NCOA4 were still the most concerned in the field of ferritinophagy research. Cancer and cancer-cells in the keywords also appear more frequently, 18 times and 12 times, respectively. And the corresponding total link strengths are 73 and 65, respectively. Therefore, it can be inferred that the research on ferritinophagy mainly focuses on basic disciplines such as cytology, cytochemistry, molecular biology, and pharmacy. However, clinical medicine mainly focuses on oncology research, which shows that ferritinophagy has great research value in the medical field.

Using Web of Science as the carrier and VOSviewer visual software for cluster analysis, this paper objectively presented the publication year, journals, countries, authors and institutions of the Ferritinophagy study, and summarized the global research hotspots in this field in the past five years. In the next step, we should promote the integration of Chinese research with international hotspot and improve the depth and breadth of Chinese research in this field. The United States was the country with the strongest comprehensive strength in the field of Ferritinophagy, and its academic output level and cooperation depth in this field far exceeded that of other countries/regions in the world. The research in the field of cancer may be the focus of Ferritinophagy's research in the future, while the researches on oxidative stress pathway, cell death mode and NCOA4 in the field of Ferritinophagy are the current hotspots and will be further studied in the future.

However, there are some limitations in this study. Only one database, Web of Science, is retrieved, and the data source is one-sided, which may omit literatures of some countries and journals. The author information in the included literature has the same name and the author institution is not unique. Although this study has been standardized, there will be some errors. For the inclusion of research literature, only the quantity of literature was considered, not the quality of literature. At the same time, the indexes involved in bibliometrics are affected by the length of literature publication. Recently published literatures may show less numerical values in various indexes due to the short

publication time, resulting in deviations in results. The development trend of ferritinophagy was not unchangeable, and it was necessary to closely follow its dynamics in the future to more accurately grasp the development trend of this field.

Author Contributions

YW and ZX takes responsibility for the integrity of the work as a whole, from inception to published article. WL and YW conceived and designed the study. WL collected and analyzed the data. WL and YW wrote the paper. YW and ZX edited the article. All authors approved the final version of the manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Li X, Lozovatsky L, Sukumaran A, Gonzalez L, Jain A, Liu D, *et al*. NCOA4 is regulated by HIF and mediates mobilization of murine hepatic iron stores after blood loss. Blood. 2020; 136: 2691–2702.

[2] Hou W, Xie Y, Song X, Sun X, Lotze MT, Zeh HJ, *et al*. Autophagy promotes ferroptosis by degradation of ferritin. Autophagy. 2016; 12: 1425–1428.

[3] Pasricha S, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. The Lancet. 2021; 397: 233–248.

[4] Mancias JD, Pontano Vaites L, Nissim S, Biancur DE, Kim AJ, Wang X, *et al*. Ferritinophagy via NCOA4 is required for erythropoiesis and is regulated by iron dependent HERC2-mediated proteolysis. eLife. 2015; 4: e10308.

[5] Fujimaki M, Furuya N, Saiki S, Amo T, Imamichi Y, Hattori N. Iron Supply via NCOA4-Mediated Ferritin Degradation Maintains Mitochondrial Functions. Molecular and Cellular Biology. 2019; 39: e00010-19.

[6] Hasan M, Reddy SM, Das NK. Ferritinophagy is not required for colon cancer cell growth. Cell Biology International. 2020; 44: 2307–2314.

[7] Khalil GM, Gotway Crawford CA. A Bibliometric Analysis of U.S.-Based Research on the Behavioral Risk Factor Surveillance System. American Journal of Preventive Medicine. 2015; 48: 50–57.

[8] Lee S. Annual report of the productivity and bibliometrics of the Korean Journal of Anesthesiology. Korean Journal of Anesthesiology. 2021; 74: 1–3.

[9] Ichhpujani P, Kalra G, Kaur R, Chahal R, Kumar S. COVID-19 and ophthalmology: a scientometric analysis. Indian Journal of Ophthalmology. 2021; 69: 1234–1240.

[10] Ahmad P, Slots J. A bibliometric analysis of periodontology. Periodontology 2000. 2021; 85: 237–240.

[11] Brandt JS, Hadaya O, Schuster M, Rosen T, Sauer MV, Ananth CV. A Bibliometric Analysis of top-Cited Journal Articles in Obstetrics and Gynecology. JAMA Network Open. 2019; 2: e1918007.

[12] van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010; 84: 523–538.

[13] Chen Y, Long T, Xu Q, Zhang C. Bibliometric Analysis of Ferroptosis in Stroke From 2013 to 2021. Frontiers in Pharmacology. 2022; 12: 817364.

[14] Chen J, Li X, Jia Y, Xia Z, Ye J. Publication Trends on Mitophagy in the World and China: A 16-Year Bibliometric Analysis. Frontiers in Cell and Developmental Biology. 2021; 9: 793772.

[15] Mancias JD, Wang X, Gygi SP, Harper JW, Kimmelman AC. Quantitative proteomics identifies NCOA4 as the cargo receptor mediating ferritinophagy. Nature. 2014; 509: 105–109.

[16] Kaur J, Debnath J. Autophagy at the crossroads of catabolism and anabolism. Nature Reviews Molecular Cell Biology. 2015; 16: 461–472.

[17] Gao M, Monian P, Pan Q, Zhang W, Xiang J, Jiang X. Ferroptosis is an autophagic cell death process. Cell Research. 2016; 26: 1021–1032.

[18] Latunde-Dada GO. Ferroptosis: Role of lipid peroxidation, iron and ferritinophagy. Biochimica et Biophysica Acta. 2017; 1861: 1893–1900.

[19] Manz DH, Blanchette NL, Paul BT, Torti FM, Torti SV. Iron and cancer: recent insights. Annals of the New York Academy of Sciences. 2016; 1368: 149–161.

[20] Seibt TM, Proneth B, Conrad M. Role of GPX4 in ferroptosis and its pharmacological implication. Free Radical Biology and Medicine. 2019; 133: 144–152.

[21] Dixon SJ, Stockwell BR. The Hallmarks of Ferroptosis. Annual Review of Cancer Biology. 2019; 3: 35–54.

[22] Zhou B, Liu J, Kang R, Klionsky DJ, Kroemer G, Tang D. Ferroptosis is a type of autophagy-dependent cell death. Seminars in Cancer Biology. 2020; 66: 89–100.

[23] Li W, Li W, Wang Y, Leng Y, Xia Z. Inhibition of DNMT-1 alleviates ferroptosis through NCOA4 mediated ferritinophagy during diabetes myocardial ischemia/reperfusion injury. Cell Death Discovery. 2021; 7: 267.

[24] Gryzik M, Srivastava A, Longhi G, Bertuzzi M, Gianoncelli A, Carmona F, *et al*. Expression and characterization of the ferritin binding domain of Nuclear Receptor Coactivator-4 (NCOA4). Biochimica Et Biophysica Acta (BBA) - General Subjects. 2017; 1861: 2710–2716.

[25] Masaldan S, Clatworthy SAS, Gamell C, Meggyesy PM, Rigopoulos A, Haupt S, *et al*. Iron accumulation in senescent cells is coupled with impaired ferritinophagy and inhibition of ferroptosis. Redox Biology. 2018; 14: 100–115.

[26] Das NK, Jain C, Sankar A, Schwartz AJ, Santana-Codina N, Solanki S, *et al*. Modulation of the HIF2alpha-NCOA4 axis in enterocytes attenuates iron loading in a mouse model of hemochromatosis. Blood. 2022; 139: 2547–2552.

[27] Belaidi AA, Masaldan S, Southon A, Kalinowski P, Acevedo K, Appukuttan AT, *et al*. Apolipoprotein E potently inhibits ferroptosis by blocking ferritinophagy. Molecular Psychiatry. 2022. (in press)

[28] Zhang Z, Yao Z, Wang L, Ding H, Shao J, Chen A, *et al*. Activation of ferritinophagy is required for the RNA-binding protein ELAVL1/HuR to regulate ferroptosis in hepatic stellate cells. Autophagy. 2018; 14: 2083–2103.

[29] Ito J, Omiya S, Rusu MC, Ueda H, Murakawa T, Tanada Y, *et al*. Iron derived from autophagy-mediated ferritin degradation induces cardiomyocyte death and heart failure in mice. eLife. 2021; 10: e62174.

[30] Yoshida M, Minagawa S, Araya J, Sakamoto T, Hara H, Tsubouchi K, *et al*. Involvement of cigarette smoke-induced epithelial cell ferroptosis in COPD pathogenesis. Nature Communications. 2019; 10: 3145.