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Global Research Trends in Single-Cell Sequencing in Degenerative Disease Research: A Bibliometric and Visualization Study

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Abstract: *The role of single-cell sequencing in degenerative diseases has attracted significant attention in current research. This study aims to investigate the global status and emerging trends in this field. The literature on single-cell sequencing in degenerative diseases was retrieved from January 1, 1991 to September 1, 2023, utilizing the Web of Science Citation Index Expanded. The source data was analyzed using bibliometric methods. To visualize the research findings, VOS viewer version 1.6.19 software was employed for co-authorship analysis, co-occurrence analysis, bibliographic coupling, and co-citation analysis. The study also evaluated the overall trend of single-cell sequencing in degenerative disease research in recent years. A total of 1430 articles were retrieved, reflecting a continuous increase in research and publications on single-cell sequencing in degenerative diseases worldwide. The United States has played a prominent role in this field, contributing the highest number of publications and citations, as well as having the highest h-index. Springer Nature and Frontiers Media Sa emerged as the leading publishers. Noteworthy contributors include the National Institutes of Health (NIH) in the USA, Nanjing Medical University, Harvard University, and the University of Texas System. The research in this field primarily focuses on three key aspects: oncology, genetics, and molecular biology. Oncology is predicted to be the next significant area of interest in single-cell sequencing research on degenerative diseases. The findings suggest that the number of publications related to single-cell sequencing in degenerative diseases will continue to increase based on current global research trends. Presently, the United States remains the primary driver of research in this field, with a focus on clinical studies, particularly in oncology, which is likely to become the next prominent topic in the realm of single-cell sequencing in degenerative diseases.*

Keywords: *Single-Cell Sequencing, Degenerative Diseases, Global Trends, Bibliometrics, Visualization Research*

1. Introduction

Degenerative diseases are prevalent in clinical practice and significantly impact quality of life. They encompass various pathological changes, including intervertebral disc degeneration, spinal stenosis, spinal instability, and bone hyperplasia [1]. Previous research on these diseases primarily focused on overall observations at the tissue and organ levels, with limited understanding at the cellular level. However, the emergence of single-cell sequencing technology in recent years has provided a new perspective for exploring the pathological mechanisms of degenerative diseases [2]. Single-cell sequencing technology offers higher resolution and sensitivity compared to traditional methods, enabling in-depth exploration of molecular differences and expression patterns between distinct cell subpopulations[3]. By utilizing this technology, we can gain a more comprehensive understanding of the occurrence and progression of degenerative diseases. This article aims to review the application of single-cell sequencing technology in studying degenerative diseases and highlight its significant achievements [4]. Specifically, we will focus on analyzing various cell types in cervical and lumbar tissues at the single-cell level and investigating their transcriptomic and epigenetic characteristics in disease occurrence and progression. Through an extensive review of existing literature, we aim to demonstrate the profound impact of single-cell sequencing technology on uncovering the mechanisms of degenerative diseases. We believe that by harnessing the power of single-cell sequencing technology, we can gain a comprehensive and profound understanding of the molecular basis and pathological processes underlying degenerative diseases[5]. This knowledge will contribute to the development of personalized treatment strategies in the future and pave the way for improved management of lumbar degenerative diseases [6].

However, the global development trend of single-cell sequencing for degenerative diseases has not been thoroughly investigated. Therefore, it is necessary to summarize the current status of single-cell sequencing research on degenerative diseases and identify potential keywords and trends. Publications serve as important indicators for measuring research contributions in scientific research. Bibliometric analysis, which utilizes literature databases and bibliometric features, allows for qualitative and quantitative evaluation of research activities over time [7]. It provides insights into the development of a specific field and facilitates comparisons of the contributions made by scholars, journals, institutions, and countries. Furthermore, bibliometric analysis is valuable for guiding policy-making and clinical practice guidelines [8].This feasible method has successfully been employed to assess research trends in osteoarthritis, hypertension, diabetes, and injury. To the best of our knowledge, no reports have examined the quantity and quality of research in the field of degenerative diseases using single-cell sequencing. Therefore, the purpose of this study is to evaluate the current research status and global trends of single-cell sequencing in the study of degenerative diseases.

2. Materials and Methods

2.1 Data Sources

Based on Web of Science Citation Index Expanded (WOS) for bibliometric analysis of data sources, this index is considered the best database for bibliometrics [9].

2.2 Search Strategy

In this study, the search terms were as follows: Subject=(single-cell sequencing + degeneration) and publication year=(1991-01-023-09-01) and Language=(English).

2.3 Data Collection

We obtained and analyzed complete detailed information (including title, publication year, author name, country, journal name, affiliation, keywords, and abstract) from the WOS database and uploaded it to Microsoft Office Mondo 2016. The two authors (HFZ and LHL) independently filter and extract, input, and collect data. Manually cleaned and analyzed data from Microsoft Office Mondo 2016 and GraphPadPrism9.

2.4 Bibliometric Analysis

Bibliometric analysis has emerged as a vital tool for conducting global investigations and analyses in various scientific disciplines. Mathematical and statistical methods have been extensively employed to examine a large body of literature and research trends [10]. The Web of Science (WOS) function is commonly employed to provide an overview of the key characteristics of the aforementioned qualified articles [11]. The h-index, which serves as an alternative measurement indicator, offers the most effective means of quantifying the impact of scientific research. Specifically, the h-index denotes that a scientist or country has published h articles that have been cited h times or more by other publications [12]. The logistic growth model: $f(x) = a/(1+ebcx)$ demonstrates robust applicability and predictive capabilities for future trends [13]. To depict the number of publications over time, a graph can be created using GraphPad Prism 9 [14]. In this graph, the independent variable x represents the year, while the dependent variable f(x) signifies the total number of publications. To examine the annual publication count, top 20 countries worldwide, authors, institutions, funding sources, research directions, total citation frequency, journals, average citation frequency, and h-index, Microsoft Office Mondo 2016 was employed for analysis [15]. For visual incorporation of publications, VOS viewer software (VOS) may be utilized, which has previously been employed for bibliographic coupling, cocitation analysis, co-occurrence analysis, and co-authorship analysis [16].

3. Results

3.1 Trends in Global Publications

3.1.1 Total Number of Global Publications

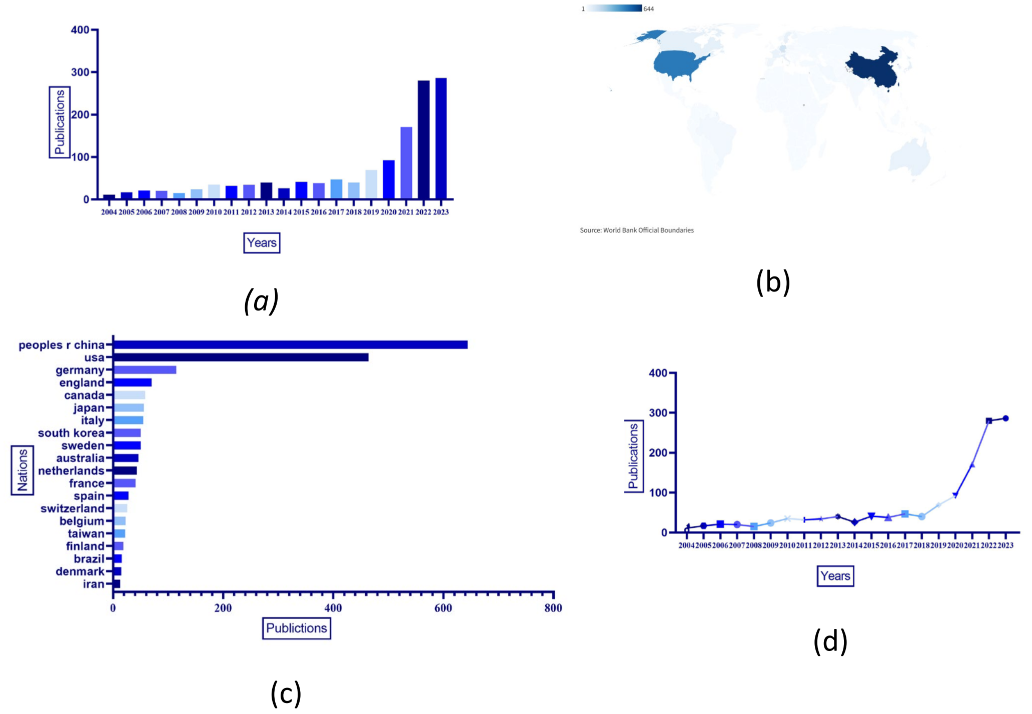
As a result, there were 1430 articles that met the search criteria in the global publication trend from January 1, 1991 to September 1, 2023. Most studies were published between 2019 and 2023 (898, 62.7%), examining the annual publication volume. From 1991 to 2023, a significant trend can be observed as the number of global publications continues to increase each year. In addition, in the past few years, the relative research interest in this field has shown an upward trend (Figure 1a).

3.1.2 Contributions of Countries

A total of 78 countries and regions have made contributions to this field. Among these countries, China has published the most relevant articles (644, 45.039%), followed by the United States (464, 32.447%), Germany (115, 8.041%), the United Kingdom (70, 4.895%), and Canada (58, 4.055%) (Figure 1b, c).

3.1.3 Global Publishing Trends

Global publication trends use logistic regression models to create a time curve of the number of publications, from which future trends can be predicted. Figure (1d) shows the fitted curve of the model for predicting the growth trend of global publication quantity in the coming years[17].



(a) The total number of publications on the research and related research interests of single-cell sequencing in degenerative diseases.(b) Research on single-cell sequencing in degenerative diseases and its related global distribution map.(c) The total number of publications related to single-cell sequencing in degenerative diseases in the top 20 countries.(d) Fitting curve for predicting the growth trend of global publication quantity in the coming years

Figure 1: Global publication trends on single-cell sequencing research in degenerative diseases and related studies

3.2 Quality of Publications in Different Countries

3.2.1 Total Citation Frequency

The total citation frequency of publication quality in different countries is the highest in the United States (19325). China ranks second in total citation frequency (4793), followed by Germany (2985), the

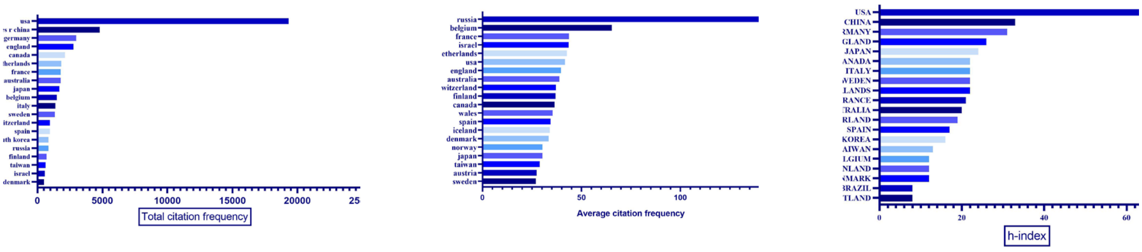
United Kingdom (2775), and Canada (2113) (Figure 2a).

3.2.2 Average Citation Frequency

The average citation frequency of Russian publications is the highest (140.16). Belgium ranks second in average citation frequency (65.34), followed by France (43.68), Israel (43.46), and the Netherlands (42.62) (Figure 2b).

3.2.3 H-index

The country with the highest h-index is the United States (68), followed by China (33), Germany (31), England (26), and Japan (24) (Figure 2c).



(a) (b) (c)

(a) Research on single-cell sequencing in degenerative diseases and its related studies Total citation frequency of national publications.(b) Research on single-cell sequencing in degenerative diseases and its related studies Average citation frequency of national publications.(c) Research on single-cell sequencing in degenerative diseases and its related research National publication H-index

Figure 2: Publication quality in different countries

3.3 Evaluation of Global Publications

3.3.1 Journal Analysis

The journal Frontiers in Immunology (Impact Factor [IF]=3.504) ranked first in research on single-cell sequencing in degenerative diseases, with 60 articles published. There are 53 articles in Frontiers in oncology (IF=2.125), 35 articles in Frontiers in genetics (IF=1.702), and 35 articles in Plos one (IF=1.755) related to the study of single-cell sequencing in degenerative diseases. The top 20 journals with the most published research are shown in Figure 3a.

3.3.2 Source of Funds

(Figure 3b) describes the top 20 sources of funding. The National Natural Science Foundation Of China Nsfc supports 264 studies (ranked first), while the United States Department Of Health Human Services supports 261 studies (ranked second).

3.3.3 Author

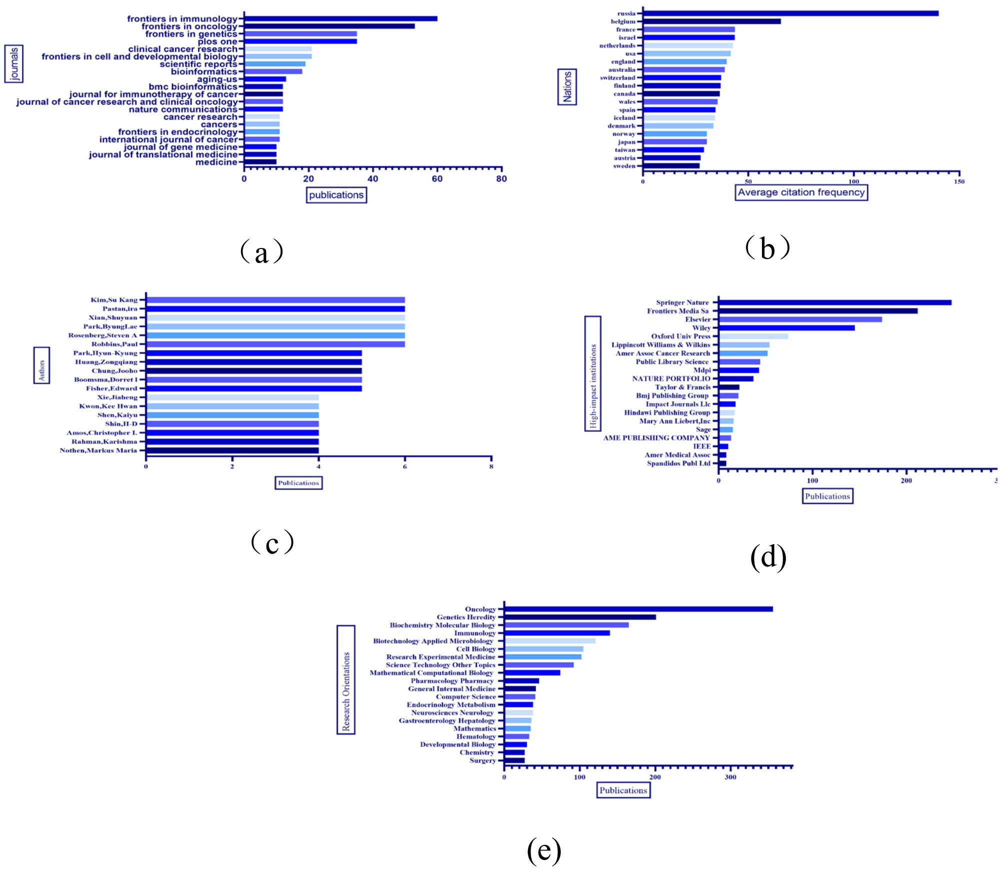
The top 20 authors have published a total of 106 articles, accounting for 7.35% of all publications in this field (Figure 3c). Kim, Su Kang published 9 articles on the study of single-cell sequencing in degenerative diseases, Pastan, ira published 8 articles, followed by Xian, Shuyuan, and Park, ByungLae each published 6 articles on the study of single-cell sequencing in degenerative diseases.

3.3.4 Publication Institutions

The top 20 research institutions have published a total of 1231 articles, accounting for 85.31% of all articles in this field (Figure 3D). Springer Nature and Frontiers Media Sa have published 248 and 212 articles respectively.

3.3.5 Research Direction

The distribution of research directions related to single-cell sequencing in degenerative diseases is shown in Figure 3e. Oncology, genetics, biochemistry and molecular biology, immunology, and biotechnology applied microbiology are the most popular research fields.



（a） （b）

（c） (d)

(e)

(a) Number of articles published in the top 20 journals on single-cell sequencing in degenerative diseases.(b) Number of published articles on single-cell sequencing related research in generative diseases from the top 20 funding sources.(c) Number of articles published by the top 20 authors on single-cell sequencing in degenerative diseases.(d) Number of articles published by the top 20 publishing institutions on single-cell sequencing in degenerative diseases.(e)Top 20 research directions

Figure 3: Evaluation of global publications on single-cell sequencing in degenerative diseases

3.4 Bibliographic Coupling Analysis

3.4.1 Journal

Use VOS viewer to analyze the journal names in all articles (defined as the minimum number of articles that are used more than 5 times) (Figure 4a). 55 recognized journals appeared in the total link strength. The top five journals in terms of total link strength are as follows: Frontiers in immunology (total link strength=8151 times), Frontiers in oncology (total link strength=7347 times), Frontiers in genetics (total link strength=5072 times), Frontiers in cell and developmental biology (total link strength=3692 times), and Journal of Cancer Research and clinical oncology (total link strength=2399 times).

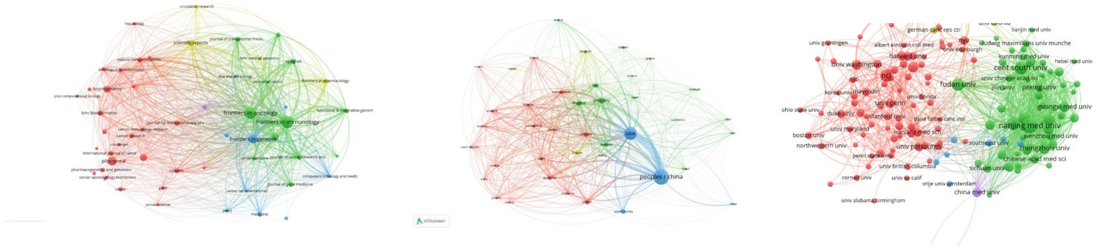
3.4.2 Country

We analyzed articles from 40 countries using VOS viewer (defined as the minimum number of articles used by a country more than 5 times) (Figure 4b). The top 5 countries in terms of total link strength are as follows: the United States (total link strength=58264 times), China (total link strength=52187 times), Germany (total link strength=23792 times), the United Kingdom (total link strength=21305 times), and Canada (total link strength=15146 times).

3.4.3 Institutions

VOS viewer was used to analyze articles from 156 institutions (defined as the minimum number of articles that institutions use more than 5 times) (Figure 4c). The top 5 institutions in terms of total link strength are as follows: Cent South University (total link strength=12934 times), Nanjing Medical University (total link strength=12548 times), University of Shanghai Jiao Tong (total link strength=11631 times), University of Zheng Zhou (total link strength=11328 times), and Southern Medical University

(total link strength=11040 times)



(a) (b) (c)

(a) Network diagram of 55 journals on the related research of single-cell sequencing in degenerative diseases.(b) Network diagram of 40 countries on the related research of single-cell sequencing in degenerative diseases.(c) Network diagram of 156 institutions related to single-cell sequencing in degenerative diseases

Figure 4: Bibliographic coupling analysis of related studies on single-cell sequencing in degenerative diseases

3.5 Co Author Analysis

3.5.1 Author

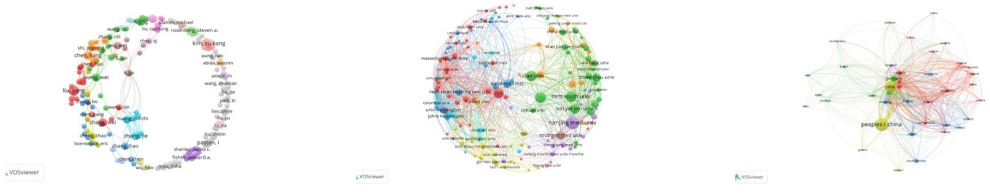
Co author analysis shows that the relevance of a project depends on the number of co authored papers; 187 authors were analyzed using VOS viewer (defined as the minimum number of articles a single author uses more than 3 times) (Figure 5a). The top five authors in terms of total link strength are as follows: Fisher, Edward A. (total link strength=33.00 times), Huang, Zongqiang (total link strength=30.00 times), Xian, Shu yuan (total link strength=30.00 times), Brown, Emily J. (total link strength=29.00 times), and Moore, Kathryn J. (total link strength=29.00 times).

3.5.2 Institutions

We analyzed studies from 156 institutions using VOS viewer (defined as the minimum number of articles used by institutions more than 5 times) (Figure 5b). The top five institutions in terms of total link strength are as follows: University of Shanghai Jiao Tong (total link strength=58.00 times), Nan Jing Medical University (total link strength=52.00 times), University of Washington (total link strength=50.00 times), Brigham&Women Hospital (total link strength=48.00 times), and Harvard Med School (total link strength=44.00 times).

3.5.3 Country

VOS viewer was used to analyze publications from 40 countries (defined as the minimum number of articles used by a country more than 5 times) (Figure 5c). The top five countries in terms of total link strength are as follows: United States (total link strength=449.00 times), Germany (total link strength=253.00 times), United Kingdom (total link strength=251.00 times), Netherlands (total link strength=198.0 times), and Canada (total link strength=175.00 times).



(a) (b) (c)

(a) Analysis of 187 co authors on single-cell sequencing in degenerative diseases.(b) Mapping of research collaboration analysis on single-cell sequencing in degenerative diseases among 156 institutions.(c) Research and mapping of single-cell sequencing in degenerative diseases through cooperation among 40 countries

Figure 5: Co authorship analysis of single-cell sequencing in degenerative diseases

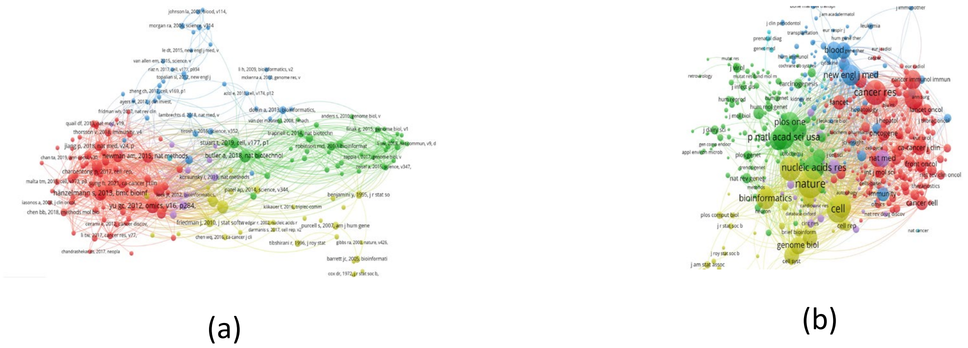
3.6 Co Citation Analysis

3.6.1 Article

According to co citation analysis, the correlation between things depends on the number of times they appear in common citations. VOS viewer is used to analyze 184 articles (defined as the minimum number of articles with more than 10 references) (Figure 6a). The following are the top 5 studies with high total link strength: H ä nzelmann s, 2013, Bmc Bioinformatics, V14, doi 10.1186/1471.2105.14.7; Yu Gc, 2012, Omics, V16, P284, doi 10.1089/omi-2011.0118; Yoshihara K, 2013, Nat Commun, V4, doi 10.1038/ncomms3612; Subramanian A, 2005, PnatlAcad Sci Usa, V102, P15545, doi 10.1073/pnas.0506580102; Butler A, 2018, Nat Biotech, V36, P411, doi 10.1038/nbt.4096.

3.6.2 Journals

Use VOS viewer to co cite and analyze journal names (defined as the minimum number of citations for a co cited journal exceeding 20 times). As shown in (6b), 501 recognized journals appeared in the total link strength. The top 5 journals in terms of total link strength are as follows: Nature (total link strength=73223 times), Cell (total link strength=62866 times), Science (total link strength=52094 times), Proceedings of The National Academy of Sciences of The United States of America (total link strength=48773 times), and Cancer Research (total link strength=47785 times).



(a) Network diagram of common cited references in this field (b) Network diagram of journals commonly cited in this field

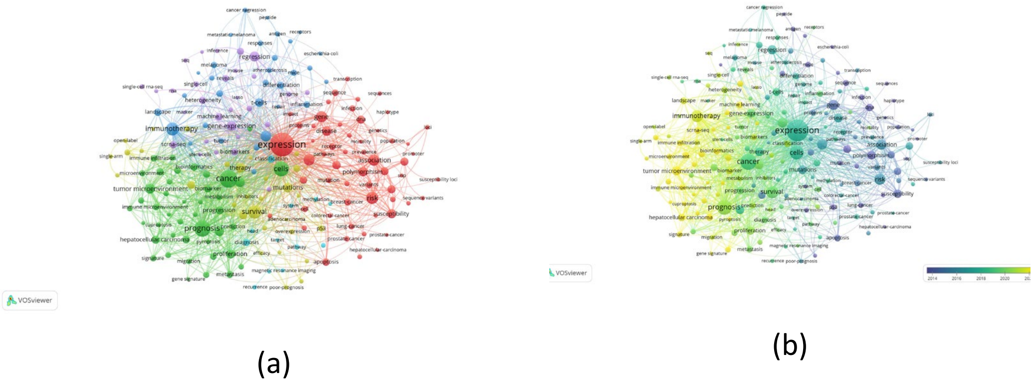
Figure 6: Co citation network diagram of single-cell sequencing in the study of degenerative diseases

3.7 Co occurrence Analysis

The purpose of co-occurrence analysis is to discover research directions and hot topics (defined as the minimum number of keywords used more than 10 times), which is even crucial for the development of scientific research directions. As shown in Figure 7a, 203 identified keywords are classified into three clusters, roughly: "presentation", "prognosis", and "cancer" (Figure 7a). In the "performance" cluster, the commonly used keywords are: classification, identification, and genes. For the "prognosis" cluster, the main keywords are: survival, tumor microenvironment, and spread. For the "cancer" cluster, the main keywords are: immunotherapy, gene expression, and prognostic models.

These results indicate that the most prominent areas in the study of single-cell sequencing for degenerative diseases include the aforementioned three directions.

VOS viewer color codes keywords based on the average time they appear in all indexed publications (Figure 7b). Blue indicates earlier appearance of keywords, while yellow indicates later appearance of keywords. Before 2016, in the early stages of research, most studies focused on presentation, prognosis, and cancer. The latest trends indicate that the second "prognostic" cluster is about to receive widespread attention in the future.



(a) Keyword network diagram of single-cell sequencing in degenerative disease research (b) Average frequency distribution network diagram of keywords

Figure 7: Co occurrence analysis of single-cell sequencing in degenerative disease research

4. Discussion

4.1 Global Publishing Status and Quality

The visualization and analysis of research references in single-cell sequencing applied to degenerative diseases can shed light on the current progress of scientific research and facilitate future predictions [18]. Thus, the objective of this study is to evaluate the impact of single-cell sequencing on the study of degenerative diseases in terms of the contributions made by countries, institutions, funding agencies, and research priorities.

Recently, the field of single-cell sequencing in degenerative diseases has witnessed exciting and rapid progress. As evidenced by this study, there has been a significant increase in the number of publications annually. Moreover, research interest in the application of single-cell sequencing in the context of degenerative diseases has experienced a sharp rise in recent years. Notably, a total of 78 countries and regions have contributed to relevant research in this field. By analyzing the available data, we are able to make predictions about future publication rates. It is expected that the coming years will witness a further surge in high-quality research promoting a deeper understanding of the role of single-cell sequencing in degenerative disease research. These promising results will, in turn, inspire researchers to conduct further rigorous investigations.

4.2 Research Trends in Single-Cell Sequencing in Degenerative Diseases

According to the analysis of national contributions, China has the highest number of publications, with the National Natural Science Foundation of China (NSFC) and the United States Department of Health and Human Services ranking first and second, respectively, in terms of research direction and funding. The United States has made the most significant contribution to the research on single-cell sequencing in degenerative diseases, with a large number of published papers. In terms of citation frequency and h-index, the United States can be considered a global pioneer and leader in this topic. China ranks second in overall publications. However, the United States ranks first in overall citation frequency and the h-index. In fact, China's academic evaluation system tends to prioritize quantity over quality, which may explain why there are differences in publication quantity and quality, leading researchers and doctors to rush to submit articles and sometimes neglect research quality. The gradually expanding research funding in China will greatly improve the quality of publications and help China keep up with the global standards in this field.

Bibliographic coupling refers to the citation of the same third book in the references of two separate books. In this study, we conducted a similarity link coupling analysis by examining the bibliographies of different articles from three perspectives: journal, institution, and country. Notably, the core journals that focus on single-cell sequencing in degenerative diseases include Frontiers in Immunology, Frontiers in Oncology, Frontiers in Genetics, Frontiers in Cell and Developmental Biology, and the Journal of Cancer Research and Clinical Oncology. These journals are known for their up-to-date coverage of research in this field. It is worth mentioning that Frontiers in Immunology and Frontiers in Oncology have the highest number of published papers, indicating their leading role in international single-cell sequencing research related to degenerative diseases. Among the institutions, Central South University stands out with the highest total link strength, making it a prominent player in single-cell sequencing research of degenerative diseases. Moreover, the top three institutions with the most published articles worldwide are all from China, which aligns with China's dominant position in this field. It is evident that the establishment of top-notch research institutions plays an essential role in elevating a country's academic standing. Figure 3c shows that Kim, Su Kang, and Pastan, Ira are the most influential contributors, warranting close monitoring of their future research and the latest developments in newly published articles on single-cell sequencing in degenerative diseases. Co-authorship and publication of papers hold great significance in fostering scientific advancement, facilitating research innovation, knowledge sharing, and improving the overall quality of scientific research. The co-author analysis approach facilitates the evaluation of collaborations among different countries, institutions, and authors. It is observed that authors, institutions, and countries with higher overall link strength exhibit a greater willingness to collaborate. For instance, Fisher, Edward A., University of Shanghai Jiao Tong, and the United States are identified as optimal choices for joint efforts. The purpose of conducting co-citation analysis is to assess the impact of a study based on the number of times it has been cited. The findings of our research demonstrate that single-cell sequencing garners a high overall citation frequency in seminal research on degenerative diseases and provides an abundance of valuable references. It is well-known that Nature and Cell are the most frequently mentioned journals in this context.

4.3 Research Focus of Single-Cell Sequencing in Degenerative Diseases

We conducted a co-occurrence analysis to identify research directions and prominent topics in this field. A co-occurrence network diagram was created using all the terms found in the research title and abstract (Figure 7a). The diagram reveals three research directions: "presentation", "prognosis", and "cancer". These studies help to clarify future research paths. Keywords such as performance, prognosis, cancer, classification, differentiation, genes, survival, tumor microenvironment, spread, immunotherapy, gene expression, and prognostic models are commonly used and hold influential positions in the co-occurrence network graphs. Thus, further high-quality research on single-cell sequencing in degenerative diseases is warranted, and these three indicators remain crucial. Overlay visualization maps, similar to co-occurrence maps, use colors to indicate the year of publication of the research. However, the colors of the projects differ, reflecting the time they occurred (Figure 7b). This method precisely directs research tracking. Based on the survey results, oncology and prognosis appear to be potential upcoming hot topics in this field.

4.4 Advantages and Limitations

This study assessed the current research progress and trends in single-cell sequencing for degenerative diseases through visual analysis. However, it is important to acknowledge the following limitations. The analysis of English language research is based on the Web of Science Science Citation Index Expanded data source[19], which could result in a language bias by excluding non-English literature. Furthermore, there may be discrepancies between the real-world scenario and the findings of this study. For instance, recently published high-quality papers might not receive sufficient attention due to their low citation frequency immediately after publication. Hence, it is crucial for researchers to remain updated with the latest primary research and consider non-English studies for a comprehensive understanding of the field.

5. Conclusion

Conclusion: This study elucidates the widespread utilization of single-cell sequencing in studying degenerative diseases. Notably, the United States has emerged as the predominant contributor to research in this field, taking a leading role in forthcoming publications on single-cell sequencing for degenerative diseases. Specifically, in the realm of oncology, single-cell sequencing is poised to receive greater attention and become a prominent area of investigation in the future [20].

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