

Bibliometric Analysis of Epididymal Sperm Maturation Over the Past 20 Years

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Abstract

Background: The epididymis, as an important male sexual organ, plays a key role in sperm transport, maturation, and storage. In recent years, the quality of male semen has been declining, and the role of the epididymis in the process of sperm maturation has gradually attracted the attention of scholars, and there is no bibliometric analysis in this field. This study aimed to conduct a bibliometric analysis of research trends in the field of epididymal sperm maturation over the past 20 years. **Methods:** The articles and reviews related to sperm maturation in the epididymis from 2003 to 2022 were searched in the WOS core database. Vosviewers, Citespace, and the bibliometrix R software packages were used for bibliometric analysis. **Results:** We found 1102 articles published in English between January 2003 and December 2022. The number of publications related to epididymal sperm maturation is slowly fluctuating and rising. The United States and China are the two countries that have published the most articles in this field, while the United States and Australia are the two countries that have been most active in international cooperation. Newcastle University, Laval University, and McGill University are the main research institutions. Biological of Reproduction is the most popular journal in the field and the most cited journal. Nixon Brett has published the most papers and Sullivan Robert has been cited the most. Through cluster analysis, it was found that the main directions of this research field are androgen receptor, oxidative stress, sperm capacitation, basal cells, gamete biology, sperm development, epigenetics, proteomics, acrosome reaction, and transgenes. Extracellular vesicles, oxidative stress, male infertility, transcriptomics, epigenetics, and epididymal head, body, and tail are emerging and important research hotspots. **Conclusion:** This paper is the first bibliometric analysis in the field of epididymal sperm maturation. This article will provide the latest research directions and hot spots, which will provide a reference for scholars studying the function of the epididymis.

Keywords

Bibliometric analysis, epididymis, sperm maturation, research hotspots, male infertility

Lay summary

This paper is the first bibliometric analysis in the field of epididymal sperm maturation. This study explains the important role of the epididymis in mirror maturation with authors, institutions, countries, journals, and key research in the last 20 years. Besides, the current research frontiers and hot areas of epididymal sperm maturation are identified, to help researchers determine the research direction and promote the development of epididymal sperm maturation.

1. Introduction

Infertility affects 8-12% of couples worldwide, Male factors account for 50%, leading to male infertility factors, spermatogenesis, and sperm maturation damage or abnormal semen quality decline is one of the male infertility factors [1]. Studies from 1981-2013 showed significant reductions in sperm concentration (SC) and total sperm count (TSC) in North American-European-Australian men, while a recent meta-analysis showed a significant decrease in semen parameters in men in South America/Central America-Asia-Africa, with mean SC decreasing by 51.6% between 1973 and 2018 and TSC by 62.3% overall in men [2]. This suggests an urgent need to study the causes of the decline in sperm quality in men and to take action to prevent further decline in male fertility. One study showed that SARS-CoV-2 disrupted the structure and function of the epididymis, resulting in impaired spermatogenesis and maturation, and male infertility [3].

The epididymis can be broadly divided into three regions, including the head, body, and tail of the epididymis. In some species, such as mice, the region of the epididymis at the proximal end is also called the initial segment [4]. Johnston et al. found that 17,000 transcript gene expression patterns in mice changed along the epididymis, suggesting that the epididymis affects sperm function [5]. The epididymis is the main site of sperm maturation. Cornwall research shows that the epididymis promotes the ability of sperm to gain progressive movement and fertilization, and plays an important role in the maturation of sperm [4]. At the protein level, Sullivan R studies have shown that the epididymis plays an important role in the endocrine vesicles and spermatozoa's acquisition of new proteins such as glycan phosphate synthesis and glycosylphosphatidylinositol-anchored proteins [6]. In addition, the epididymal environment also affects sperm maturation. Intralumen bicarbonate in the epididymis reduces adenylate cyclase activity, which lowers intracellular cAMP levels, and keeps sperm at rest during transport and storage in vivo, and low concentrations of calcium in the lumens help keep sperm motility at rest [7]. Sharma U showed that the epididymis is transported to mature sperm through vesicles during sperm maturation, affecting sperm small RNA transfer [8]. In conclusion, the epididymis plays an important role in sperm maturation.

However, there are data on key markers of sperm maturation, and there are few studies on the diagnosis and treatment of epididymal dysfunction, which have not been applied clinically [9]. Bibliometrics, on the other hand, is a statistical analysis method that analyzes the output and status of publications in a specific field of study from both quantitative and qualitative perspectives, to obtain important information about countries, institutions, authors, keywords, journals, references, etc [10]. However, there is still no bibliometric analysis of the field of epididymis research, autofill this knowledge gap, this study aims to conduct a bibliometric analysis of publications on epididymal sperm maturation in the past two decades (2003-2022), analyze research hotspots and priorities, and identify key contributors and current research status.

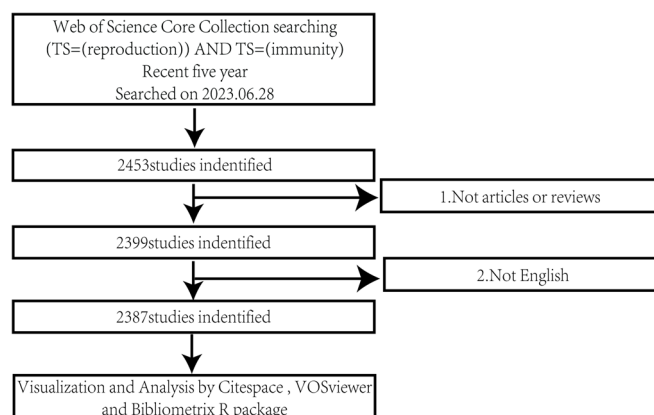


Fig. 1. Publications screening flowchart.

2. Materials and methods

2.1 Data search strategy

We searched on the Web of Science Core Collection on May 18, 2023. The search formula is ((TS = (epididymis)) AND TS = (sperm maturation)), and the language is English and the document type is article and review among all the literature obtained. In the end, we received 1102 publications.

2.2 Data analysis and visualization

For the objectivity of data analysis and the diversity of visualization, we use VOSviewer (version 1.6.19), Citespace (6.1.R3), and the Bibliometrix R package for analysis and visualization.

VOSviewer is a free computer program that specializes in the visual analysis of bibliometric maps [11]. Citespace was developed by Professor Chaomei Chen to divide the field of literature research and provide practical connections between scientific research [12]. The Bibliometrix R package was developed by Aria Massimo and Cuccurullo Corrado [13]. VOSviewer is used to analyze the contributions and collaborations of co-authors, institutions, and countries to visually analyze publications, and journals, and identify journals and publications that have a profound impact on the field. Citespace is used to draw journal double-graph overlays, timeline evolution, and keyword bursting of cluster research directions, to analyze the shift in the field's center of gravity and identify the hot research directions in the field. In addition, we used Bibliometrix to analyze the overall situation of 1102 publications, rank the influence of scholars, build a regional cooperation network, analyze the citation of publications and the impact of journals in the field, and determine the key research directions in the field.

3. Results

3.1 Overall analysis

The overall picture of the data was assessed using Bibliometrix (Fig 2 A-C). The number of publications related to epididymal sperm maturation in the WOSCC database fluctuated, with the lowest number of articles published in 2013 (n=31) and a peak in 2020 (n=73). From 2013 to 2022, the number of publications in this field fluctuated upward (Fig 2 A). From 2003 to 2016, the average citation frequency of publications per year mainly showed an upward trend, peaked in 2016 (n=3.8), and gradually decreased after 2018 (Fig 2 B). Fig 2C shows the relationship between publication references, author keywords, and publication journals. These 10 references are mainly cited in publications with the keywords of the epididymis, sperm maturation, spermatozoa, male reproductive tract, testes, spermatogenesis, and fertility, most of which are accepted by the journal *Biology of Reproduction*.

3.2 Co-author

VOSviewer visually analyzes co-authors (Fig 2 DE) and Bibliometrix ranks authors on the H-index (Fig 2 F) to showcase influential scholars in the field.

A total of 4596 scholars have been involved in the field of epididymal sperm maturation, and Fig 2D and Fig 2E demonstrate the contributions and collaborative networks of 103 scholars who have published at least 5 publications. Nixon Brett has the largest node, indicating that he has produced the most relevant publications. In addition, we observed close collaboration between multiple authors. For example, Nixon Brett actively collaborates with Liu Qiang, Dun Matthew D, and others. Fig 2F shows the top 10 cited scholars in this field, indicating the influence of scholars in the field. For example, Sullivan R was cited the most frequently, indicating that Sullivan R has a large contribution to epididymal sperm maturation and has a profound impact.

3.3 Co-authored countries and institutions

Visual analysis of institution-country co-authorship using VOSviewer (Fig 3 ABD). Use Bibliometrix to build a map of world country cooperation (Min edges = 4), with colors representing the number of papers published by countries and inter-country connections representing country cooperation (Fig 3 C).

Fig 3A means that the Chinese Academy of Sciences, UNIV LAVA, UNIV NEWCASTLE, and MCGILL UNIV have made outstanding contributions to this field. Fig 3B shows that UNIV NEWCASTLE is closely associated with other institutions, and Harvard Medical School has recently actively collaborated in this field. The United States, China, and Canada are the three countries that contribute the most in this field, of which the United States

China, and Canada all cooperate closely, while Canada and China have very little cooperation. Figure D shows that China has begun to actively cooperate with other countries in recent years. Among the top 10 countries, Australia, the United States, Germany, France, Italy, and other countries have close international cooperation, while China and India currently have a lower degree of international cooperation than other countries. Australia, France, the United States, and other countries have a higher average citation frequency, of which France has an average of 60.2 citations per article, while Chinese and Indian publications have an average citation of 14.5 and 10.8 respectively. This shows that increased international cooperation can help to increase national influence in this area.

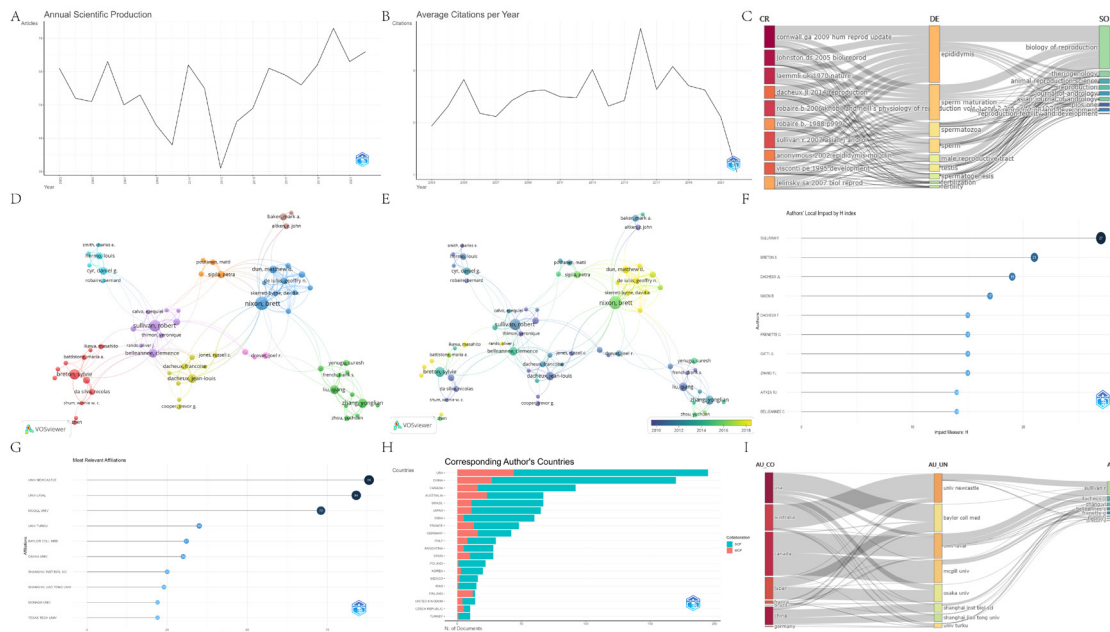


Fig. 2. Overall analysis and the brief visualization of authors, countries, and institutions. **A:** Annual scientific publication; **B:** Average citations per year; **C:** Three-field plot (CR=references, DE=keywords, SO=sources); **D:** Network visualization of co-authors; **E:** Overlay visualization of co-authors; **F:** Authors' local impact by H index; **G:** TOP 10 most relevant affiliations; **H:** Corresponding author's countries; **I:** Three-field plot (AU_CO=countries, AU_UN=affiliations, AU=authors).

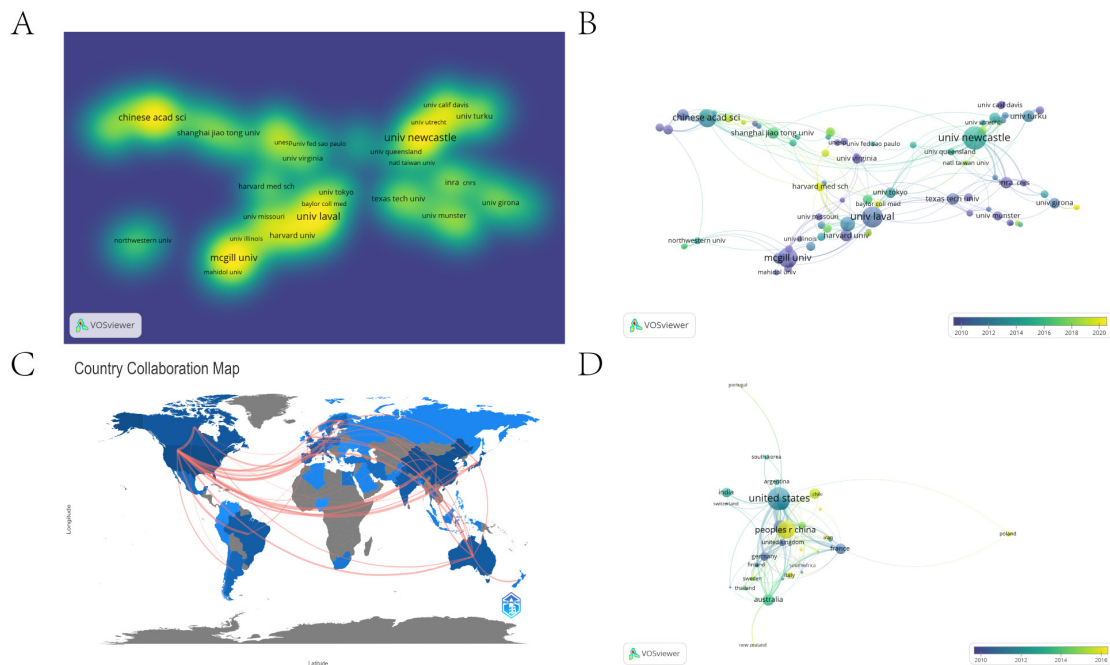


Fig. 3. The visualization of countries and institutions **A:** The distribution of institutions; **B:** The cooperation network of institutions; **C:** The geographical distribution of different regions; **D:** The cooperation network of different regions.

3.4 Publication and references

The Bibliometrix R package was used to analyze 1102 articles or reviews in the field and in all areas that influenced the top 10 publications (Fig 4 AB). Visual analysis of publication citation networks using VOSviewer (Fig 4 C).

CORNWALL GA, 2009, HUM REPROD UPDATE with 152 Local Citations is the most influential publication in the field out of 1102 publications, while SHARMA U, 2016, SCIENCE is the most influential of all areas out of 1102 publications, and Global Citations are 719. IN ADDITION, CORNWALL GA, 2009, HUM REPROD UPDATE, AND SHARMA U, 2016, SCIENCE HAVE A POSITIVE CORRELATION.

Table 1. TOP 10 most locally cited documents

Document	DOI	Year	Local Citations	Global Citations	LC/GC Ratio (%)	Normalized Local Citations	Normalized Global Citations
CORNWALL GA, 2009, HUM REPROD UPDATE	10.1093/humupd/dmn055	2009	152	392	38.78	16.08	10.04
JOHNSTON DS, 2005, BIOL REPROD	10.1095/biolreprod.105.039719	2005	98	187	52.41	9.32	3.48
SULLIVAN R, 2007, ASIAN J ANDROL	10.1111/j.1745-7262.2007.00281.x	2007	87	195	44.62	9.04	5.41
DACHEUX JL, 2014, REPRODUCTION	10.1530/REP-13-0420	2014	80	190	42.11	16.51	8.17
JELINSKY SA, 2007, BIOL REPROD	10.1095/biolreprod.106.057323	2007	75	147	51.02	7.8	4.08
DACHEUX JL, 2003, MICROSC RES TECHNIQ	10.1002/jemt.10312	2003	74	158	46.84	9.65	3.88
SULLIVAN R, 2005, BLOOD CELL MOL DIS	10.1016/j.bcmbd.2005.03.005	2005	70	224	31.25	6.66	4.16
REJRAJI H, 2006, BIOL REPROD	10.1095/biolreprod.105.049304	2006	66	146	45.21	7.27	3.72
ZHOU CX, 2004, NAT CELL BIOL	10.1038/ncb1127	2004	64	205	31.22	7.11	4.44
SULLIVAN R, 2013, REPRODUCTION	10.1530/REP-13-0058	2013	59	203	29.06	7.75	6.1

Table 2. TOP 10 most globally cited documents

Paper	DOI	Total Citations	TC per Year	Normalized TC
SHARMA U, 2016, SCIENCE	10.1126/science.aad6780	719	89.88	23.61
CORNWALL GA, 2009, HUM REPROD UPDATE	10.1093/humupd/dmn055	392	26.13	10.04
VERNET P, 2004, MOL CELL ENDOCRINOL	10.1016/j.mce.2003.10.069	352	17.6	7.62
SULLIVAN R, 2005, BLOOD CELL MOL DIS	10.1016/j.bcmbd.2005.03.005	224	11.79	4.16
JENSEN MB, 2010, HUM REPROD	10.1093/humrep/deq024	212	15.14	5.77
ZHOU CX, 2004, NAT CELL BIOL	10.1038/ncb1127	205	10.25	4.44
SULLIVAN R, 2013, REPRODUCTION	10.1530/REP-13-0058	203	18.45	6.1
SHARMA U, 2018, DEV CELL	10.1016/j.devcel.2018.06.023	196	32.67	10.62
SULLIVAN R, 2007, ASIAN J ANDROL	10.1111/j.1745-7262.2007.00281.x	195	11.47	5.41
PELLATI D, 2008, EUR J OBSTET GYN R B	10.1016/j.ejogrb.2008.03.009	195	12.19	5.02

Table 3. TOP 10 most locally cited references

Cited References	Citations
CORNWALL GA, 2009, HUM REPROD UPDATE, V15, P213, DOI 10.1093/HUMUPD/DMN055	152
JOHNSTON DS, 2005, BIOL REPROD, V73, P404, DOI 10.1095/BIOLREPROD.105.039719	98
LAEMMLI UK, 1970, NATURE, V227, P680, DOI 10.1038/227680A0	98
ROBAIRE B, 2006, KNOBIL AND NEILL'S PHYSIOLOGY OF REPRODUCTION, VOLS 1 AND 2, 3RD EDITON, P1071	96
SULLIVAN R, 2007, ASIAN J ANDROL, V9, P483, DOI 10.1111/J.1745-7262.2007.00281.X	87
DACHEUX JL, 2014, REPRODUCTION, V147, PR27, DOI 10.1530/REP-13-0420	80
ROBAIRE B., 1988, P999	76
JELINSKY SA, 2007, BIOL REPROD, V76, P561, DOI 10.1095/BIOLREPROD.106.057323	75
JONES R, 1998, J REPROD FERTIL, P73	75
DACHEUX JL, 2003, MICROSC RES TECHNIQ, V61, P7, DOI 10.1002/JEMT.10312	74

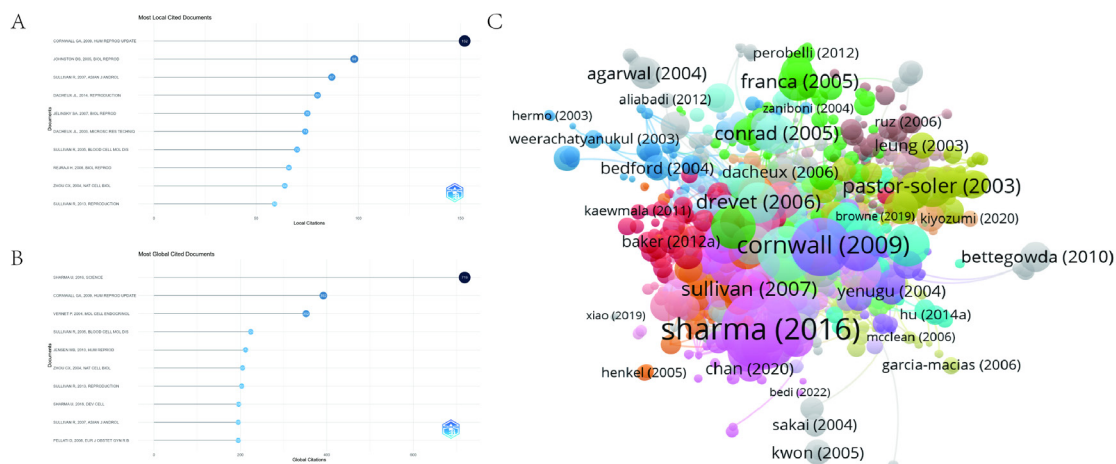


Fig. 4. Important documents and references A: Top 10 Most Local Cited Documents; B: Top 10 Most Global Cited Documents; C: Network Visualization of Documents citation.

3.5 Published and cited journals

Bibliometric analysis was used to obtain the top 10 influential journals in the field, the core journals based on Bradford's Law, and the annual cumulative number of publications in the field (Fig 5 A-C). Use Citespace to construct a two-image overlay of journals, with cited documents on the left side of the picture and cited documents on the right (Fig 5 D). Use VOSviewer for document coupling and co-citation analysis of journals (Fig 5 E).

Fig 5A shows that the top 10 journals in this field are BIOLOGY OF REPRODUCTION, ASIAN JOURNAL OF ANDROLOGY, REPRODUCTION, JOURNAL OF ANDROLOGY, PLOS ONE, MOLECULAR HUMAN REPRODUCTION, MOLECULAR REPRODUCTION AND DEVELOPMENT, THERIOGENOLOGY, ANIMAL REPRODUCTION SCIENCE, MOLECULAR AND CELLULAR ENDOCRINOLOGY. Fig 5B indicates that the core journals in the field are BIOLOGY OF REPRODUCTION, THERIOGENOLOGY, ASIAN JOURNAL OF ANDROLOGY, REPRODUCTION, ANIMAL REPRODUCTION SCIENCE, JOURNAL OF ANDROLOGY, MOLECULAR REPRODUCTION AND DEVELOPMENT, REPRODUCTION FERTILITY AND DEVELOPMENT. Fig 5C shows that the Journal of Biology of Reproduction contains the most relevant articles, and the number of articles in this field included in the Asian Journal of ANDROLOGY has remained unchanged in recent years. Fig 5D shows that Molecular, Biology, and Immunology is the application field of epididymal sperm maturation, and Molecular, Biology, Immunology, and Health, Nursing, and Medicine are the basis of research in this field. Fig 5E shows that Biology of Reproduction has a significant co-citation relationship with journals such as the Journal of Reproduction Fertility. Nature, Science, and Cell have positive co-citation relationships with journals such as Plos One. Fig 5F shows that in recent years, journals such as Andrology, International Journal of Molecular Sciences, Scientific Reports, Frontiers in Cell and Developmental Biology, Animals, and other journals have similar content in this field.

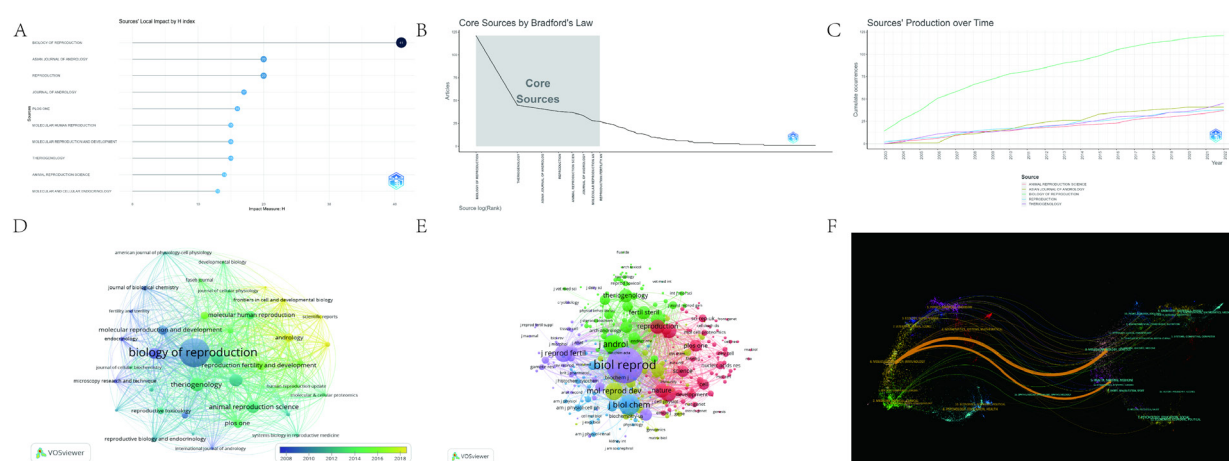


Fig. 5. Influential journals and visualization of journals A: Top 10 journals in the field based on the H index; B: The core journal in the field calculated based on Bradford's Law; C: The line chart of the production of the source over time; D: The Bibliographic coupling of documents; E: The Co-citation of Cited references; F: The dual-map overlay of journals on the research of sperm maturation in epididymis sperm maturation.

3.6 Field hotspots and key research directions

Citespace was used for timeline analysis (Fig 6 A) and keyword mutation analysis (Fig 6 C), and the Bibliometrix R package was used to draw Trend Topics (Fig 6 B) and Thematic Map (Fig 6 D).

After generating the keyword cluster map, the cluster number is used as the Y axis, the citation year is used as the X axis, and the timeline map of the co-cited network is laid out to show the period and research process of the development and evolution of each cluster. For example, the field represented by epigenetics in cluster #6 at the top, which spans from 2003 to 2022, has a series of important milestone research directions, and its association with fertilization ability has become a new hot direction in 2022. Both Fig 6B and Fig 6C show the evolution trend of keyword popularity, such as oxidative stress, extracellular vesicles, male infertility, transcriptomics, epigenetics, exosomes, etc. are hot topics in recent years. Fig 6D abscissa represents the degree of importance, and the ordinate represents the research heat, so epididymal anatomy, head body tail, oxidative stress, male reproduction, and sperm function have become the focus of this field, and microRNA and sperm morphology may be emerging fields or outdated topics.

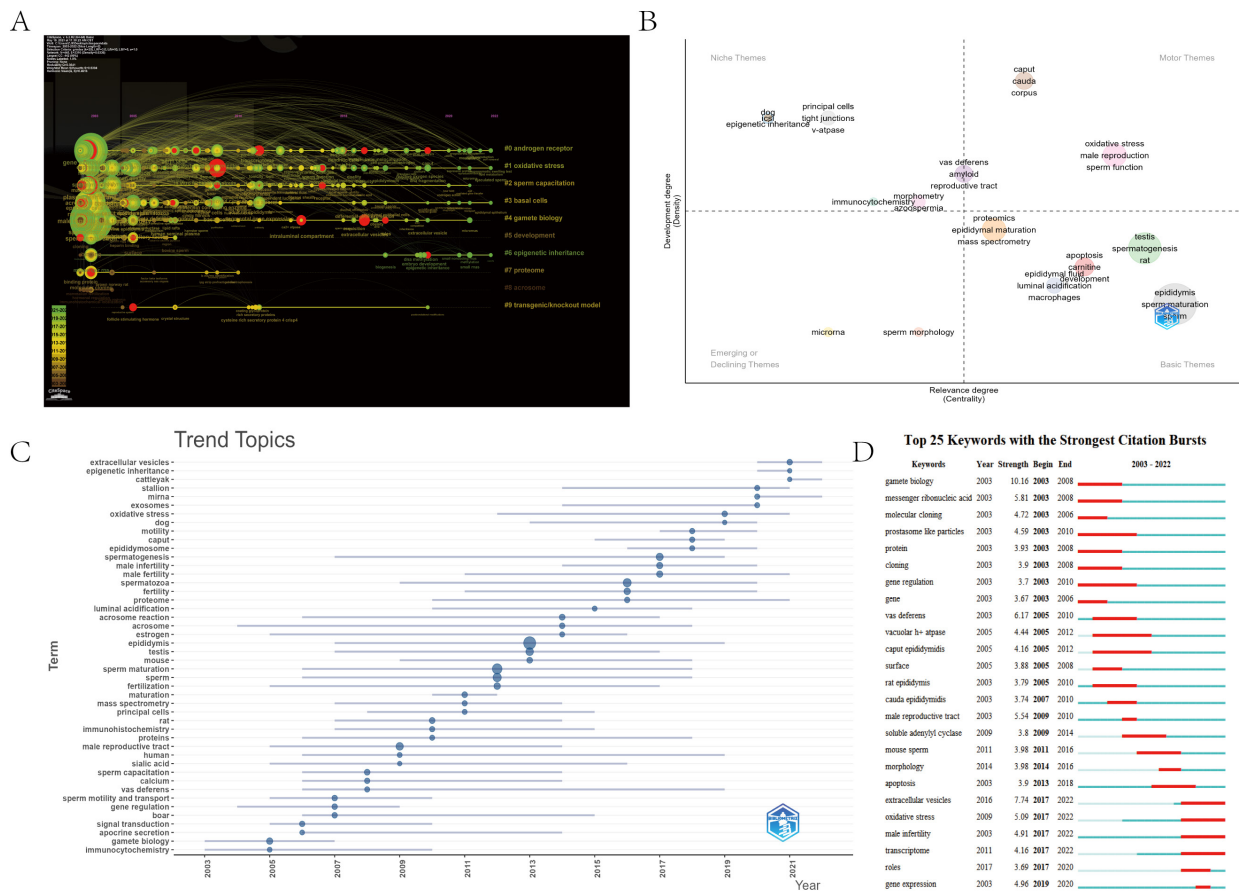


Fig. 6. Research hotspots and trends in the field A: Keywords grouped in ten clusters, timeline distribution of the top ten clusters and keywords trends by year; B: Thematic Map of Authors' keywords; C: Trend Topics of Authors' keywords; D: Top25 Keywords with the Strongest Citation Bursts.

4. Discussion

4.1 Overall

The analysis of this paper found that the research on epididymal sperm maturation from 2003 to 2022 was uninterrupted, reaching a trough in 2013 and a peak in 2020. In terms of research hotspots, topics such as androgen receptors, oxidative stress, and epigenetics have become research hotspots, and keywords such as extracellular vesicles, transcriptome, and male infertility have become increasingly prominent. The research team and authors are mainly gathered in the United States, China, Canada, Australia, and other countries, and the journal is mainly published in *Biology of Reproduction*.

4.2 Study authors, institutions, countries, and journals

From the authors' analysis results, Sullivan R (CANADA, UNIV LAVAL) and Nixon B (AUSTRALIA, UNIV NEWCASTLE) contributed the most to the field. Sullivan R is the most cited research in this area. His three articles published in 2005, 2007, and 2013 were included in the Top 10 Local and Global Citations. Sullivan R described the role of exosomes on sperm maturation during the crossing of the male reproductive tract in 2005 [14]. Then, in 2007, he elucidated the epididymis's role in acquiring new sperm proteins [6]. In 2013, Sullivan R elucidated the important role of naturally occurring extracellular vesicles and artificial vesicle liposomes in male reproductive health in the epididymis and prostate [15].

From an institutional point of view, UNIV NEWCASTLE, UNIV LAVAL, and MCGILL UNIV-related publications are the most, of which UNIV CASTLE published articles rapidly after 2014 and surpassed UNIV LAVAL in 2020. However, in recent years, the institution has had little international cooperation, which is not conducive to scientific progress in the field in the long run. From a country perspective, most of the corresponding authors are

located in the United States, China, and Canada. The United States continues to publish more publications in this field than other countries, but the number of publications in China has increased rapidly after 2019. Among the ten countries with the most publications in this field, France, the United States, Italy, Australia, and Germany actively carry out international cooperation, while India and China have a lower degree of international cooperation than other countries. The United States was the country that contributed the most to citations for publications in this field (n=8694). This seems to indicate that international cooperation is conducive to promoting the development of disciplines, so we strongly call for extensive cooperation and exchanges among research institutions in various countries to jointly promote the development of epididymal sperm maturation.

From a journal perspective, *Biology of Reproduction* has the greatest influence in this field. *Biology of reproduction*, *Theriogenology*, *Asian journal of andrology*, *Reproduction*, and other journals receive the number of publications in this field that is increasing year by year, among which *Biology of reproduction* is much higher than other journals. The superposition of the double chart of the journal shows that the research fields of the epididymis and sperm maturation are Molecular, Biology, and Immunology, which have not yet been applied to clinical practice, and most of them are in the basic research stage.

4.3 Field Research Fundamentals

The TOP10 citation references mainly focus on transcription and protein, elucidate the important role of the epididymis in sperm maturation, and discuss the influence of epididymis on sperm gene expression patterns. Cornwall's most cited co-citation reference published in the 2009 journal *Hum Reprod Update* describes the development of the epididymis, the role of the lumen microenvironment in sperm maturation, regulation, and new mechanisms by which the epididymis functions, which has led to significant advances in understanding epididymal function [4]. Johnston et al. published this study in *Biol Reprod* in 2005, analyzing the differences in gene expression of 17,000 transcripts in different locations in the epididymis from the transcriptome of mice, laying the foundation for studying the biological factors that mediate the sperm maturation of the epididymis [5]. Laemmli's work published in *Nature* in 1970 was widely cited in publications in the field, focusing on the cleavage of structural proteins during the assembly of bacteriophage T4 heads [16]. Sullivan's review shows that epididymal cells are vesicles secreted in the area of the epididymis in a far-secreted manner that play an important role in the acquisition of new proteins by mature sperm [6]. Dacheux discusses the latest relevant results of various cellular processes that occur at the sperm level in different species, presenting new insights into the function of epididymal sperm maturation [7]. Jelinsky et al. elucidated the whole gene expression pattern of rat epididymis and conducted a new evaluation with the conserved and non-conserved gene expression patterns of mice, laying the foundation for future research on biological factors that mediate sperm maturation and storage [17]. Dacheux discusses the contribution of epididymis-secreted proteins to sperm maturation and identifies the correlation between epididymis and sperm survival and fertility potential [18].

4.4 Hot and cutting-edge

Studies in the field of epididymis and sperm maturation are divided into ten clusters, namely androgen receptor, oxidative stress, sperm capacitation, basal cells, gamete biology, development, epigenetics, proteomics, acrosome reaction, and transgenes. Among them, androgen receptors, oxidative stress, and epigenetics are the current hot directions.

Androgens are essential in male reproductive health. The tail of the epididymis is an important site for storing sperm, and its function depends on the diffusion of androgens through the stromal tissue to the epithelial cells, The epididymal cells and androgen receptors are damaged after the use of disruptors, resulting in male dysfunction and apoptosis of epithelial cells [19]. Zhang, FP, and other studies have also shown that the lack of male hormone receptors leads to epididymal dysfunction, which causes male infertility [20]. However, expression levels of androgen receptors in epididymis did not differ between age groups [21]. In addition, androgen receptors have been identified as the most important upstream factors in regulating sperm orthogonal stem cell self-renewal and sperm cell proliferation [22]. Androgens upregulate nuclear progesterone (Pgr) expression in Leydig cells, promoting sperm proliferation, and potential interactions between E2/Era and the 17,20 β P/Pgr pathway maintain sperm renewal [23].

Oxidative stress is caused by environmental pollutants, chemotherapy and other chemicals, smoke, toxins, radiation, and disease that causes damage to sperm quality by reducing sperm motility and increasing DNA oxidation levels, causing male infertility [24]. Mammalian sperm maturation is mainly regulated by exosomes secreted by

epididymal epithelial cells into the lumen, and oxidative stress in the epididymal microenvironment induces endoplasmic reticulum stress of epididymal epithelial cells, changes the exon content and quantity of endoplasmic reticulum protein, and ultimately leads to abnormal sperm maturation and fertility [25]. Further maturation of sperm occurs in the epididymis and may be exposed to a large amount of oxidative stress, and to avoid damage from reactive oxygen species, both sperm and epididymis produce antioxidant molecules that protect these cells [26]. Exosomes play an important role in biological oxidative stress. Exosomes contain lipids, proteins, microRNAs, and mRNAs, and are known to play an important role in intracellular communication, with most of the proteins associated with epididymal exosomes being transferred to sperm subcells or membrane domains, preventing oxidative stress [27].

The epididymis alters the epigenetic characteristics of spermatozoa and participates in the cross-representative inheritance of paternal traits [28]. Previous studies have shown that mouse sperm acquire small RNAs from epidermal epithelial cell secretors, and these "exogenous" small RNAs act as epigenetic information carriers, mediating the transmission of paternal traits [29]. The latest research shows that sperm exchange small RNAs with cytoplasmic droplets rather than epithelial cells [30]. In addition, studies have found that the DNA methylation pattern of sperm in the stage of epididymis maturation changes, and the gradual changes of multi-histone post-translational modifications such as H3K4me1, H3K27ac, and H3K79me2, while the change of histone post-translational modifications is a core feature of epididymal sexual maturation [31]. In summary, the epididymis is involved in changes in sperm epigenetic characteristics, affecting sperm maturation.

4.5 Summary

In recent years, the number of publications in the field of epididymal sperm maturation has gradually increased, the number of citations has continued to decline, and the research direction has been clustered into ten major fields such as androgen receptor, oxidative stress, and epigenetics, and the competition between new ideas in the field of epididymal sperm maturation is fierce, which is of great significance for the discovery of new theories. Through bibliometric analysis, this study identified the current research frontiers and hot areas of epididymal sperm maturation, to help researchers determine the research direction and promote the development of epididymal sperm maturation.

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