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ORIGINAL RESEARCH

# Unlocking the Diagnostic and Therapeutic Potential of microRNA in Diabetes: A Bibliometric and Visualized Analysis (2003–2023)

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**Background:** MicroRNAs (miRNAs) hold considerable therapeutic potential for diabetes mellitus (DM). Over the past few decades, substantial progress has been made in miRNA-related diabetes research; however, comprehensive bibliometric analyses in this field remain limited. This study aims to comprehensively review the research status of miRNAs in DM, including the contributions of countries, institutions, authors and published journals, and explore the latest progress, research hotspots, and future trends.

**Methods:** Bibliometric analysis was conducted using CiteSpace and VOSviewer by searching relevant literature in the Web of Science Core Collection (WOSCC). With 5197 relevant publications retrieved from January 1, 2003, to October 31, 2023, the field of miRNAs in DM witnessed a generally upward trend in global publications.

**Results:** Global publications on miRNAs in DM showed a sustained upward trajectory. China led in publication output and influence, likely linked to its high DM prevalence. Cluster analysis identified diabetic retinopathy and diabetic nephropathy as primary research foci among co-cited studies. Keyword analysis emphasizes the top 10 words like miRNA, expression, biomarker, insulin resistance, diabetes, diabetes nephropathy, apoptosis, cell, and oxidative stress.

**Conclusion:** Research on miRNAs in DM has grown significantly, with emphasis on understanding pathogenesis and identifying therapeutic targets. This field will be further studied and translated into clinical practice in the future.

**Keywords:** microRNAs, diabetes mellitus, bibliometric analysis, T1DM, T2DM, diabetic complications

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## Introduction

Diabetes mellitus (DM) is a syndrome of metabolic abnormalities characterized by hyperglycemia. It is caused by a variety of pathogenic factors. Diabetes mellitus can be mainly classified into type I diabetes mellitus (T1DM, caused by a decrease in insulin production by pancreatic β-cells) and type II diabetes mellitus (T2DM, caused by a decrease in insulin sensitivity).[1] Due to the changes in modern lifestyle, the number of people bearing DM has increased dramatically, making it a global epidemic. The total number of people with DM worldwide will steadily increase from 578 million to 700 million, accounting for 10.9% of the total global population.[2] Diabetes has become one of the most common and fastest-growing diseases in the world. The development of diabetes is often accompanied by vascular complications, which can lead to heart failure, stroke, blindness, lower limb amputation, renal failure, etc, seriously affecting the quality of life of patients. Data show that vascular

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complications, especially ischemic heart disease, are the main cause of morbidity and mortality in diabetic patients.[3] The treatment of this chronic disease poses an enormous healthcare problem worldwide. Not only does it pose unprecedented challenges to healthcare systems, but it also imposes a severe economic burden on patients. The pathologic processes by which diabetes occurs and causes various complications have been the focus of research. Recent studies have pointed to novel roles for microRNAs in endothelial cells and arterial smooth muscle cells (SMCs), the importance of the tissue environment on cellular responses, and the unknown role of adipose tissue in regulating human endothelial cell responses.[4] In a study on microRNA-138, researchers found that it regulates hypoxia-induced endothelial cell dysfunction by targeting S100A1.[5] Another study on gestational diabetes mellitus (GDM), it was found that GDM can impair fetal umbilical vein endothelial (HUVEC) function by upregulating miR-101.[6]

MicroRNAs (miRNAs) are a class of small, naturally occurring non-coding RNAs, consisting of roughly 21–25 nucleotides, which act as a class of gene expression regulators, functioning at the post-transcriptional level to pathologically fine-tune the expression of protein-coding genes.[7] Its nature is stable, not easily degraded, and it can circulate stably in the bloodstream and retained for a long time to play a regulatory role.[8] With the rise in morbidity in recent years, increasing studies have shown that many miRNAs in blood play important roles in the pathogenesis of various diseases. For example, miRNAs are key regulators of the progression of diabetes mellitus, which is mainly manifested in pancreatic β-cell damage and insulin resistance. In addition, they are also closely associated with DM-related complications, such as diabetic nephropathy, diabetic retinopathy, and diabetic cardiomyopathy.[9] MiRNAs are promising biomarkers and targets for the diagnosis and treatment of DM.[10,11]

Bibliometrics is a discipline that focuses on the literature system and the characteristics of bibliometric data as its object of study. It employs mathematics, statistics, and other measurement techniques to investigate the quantitative relationships, analytical structures, and quantitative management of literature and intelligence. Furthermore, it aims to explore and understand certain structures, characteristics, and laws of science and technology. Bibliometrics enables the utilization of software to compile selected literature, process complex knowledge fields through information processing and knowledge measurement techniques, and subsequently employ visual mapping to uncover the dynamic laws governing the evolution of subject areas. It further showcases the authors, countries, disciplinary teams, highly cited articles, and keywords, along with other pioneering information pertinent to these fields, thereby facilitating the prediction of cutting-edge areas and development trends within the relevant domains. Additionally, it aids in the identification of research hotspots and provides a foundational literature base for the advancement of these fields. It provides a literature base for the development of various fields and an effective reference for subsequent research.[12]

Although numerous research findings have established the significant potential of miRNAs in the diagnosis and treatment of DM, a more systematic literature synthesis is needed to consolidate knowledge in this area. To enhance our understanding of miRNA applications in DM, this study employs bibliometric analysis. Utilizing relevant literature from the Web of Science (WOS) database spanning January 1, 2003, to October 31, 2023, we analyze research directions, authors, countries/regions, and other key aspects. Our aim is to summarize the development and evolution of the miRNA-DM research field across different periods, identify research hotspots, track recent progress, and pinpoint innovative directions. Ultimately, this study seeks to provide researchers with insights into the latest advancements and emerging trends in miRNA-DM research, facilitating innovation and offering a scientific foundation for improving the prevention and treatment strategies for DM patients.

# Method

## Data Collection

The core database of the Web of Science (https://login.webofknowledge.com/) was elected as the main database of our research. All the literature and papers on miRNAs in DM indexed from 2003–2023 were systematically searched by the search formula compiled as TS = (miRNA OR microRNA OR miRNAs OR micro RNA OR miR-1* OR miR-2* OR miR-3* OR miR-4* OR miR-5* OR miR-6* OR miR-7* OR miR-8* OR miR-9*) AND TS = (diabetic* OR diabetes* OR antidiabetic* OR anti-diabetic*) AND DT = (Article OR Review) AND LA = (English) AND DOP = (2003–01-01/2023-10-31). Notably, all diabetes-related complications are involved to ensure a decent analysis of the applications of miRNAs in DM. The collection was completed on October 31, 2023 to minimize potential discrepancies due to database updates. A total of 6213 publications were initially identified through the WOSCC database search. Only articles and reviews published in English that met the theme of miRNAs in DM were selected for further analysis, while book chapters, proceedings papers, meeting abstracts, corrections, editorials, duplicates, retractions, or unpublished articles were excluded. Two independent investigators (Jiajing Yu and Guanyi Xiao) retrieved and filtered the publications to ensure the accuracy of the scientometric analysis. After excluding papers irrelevant to the topic (n = 1016), 5197 research articles were identified as entitled to our study, consisting by articles (n = 4307) and reviews (n = 890), and the specific identifying process will be put forward in Figure 1A. Publication amounts and years, total and average citations, titles, countries and institutions, authors, journals, keywords, and references were all collected and analyzed.

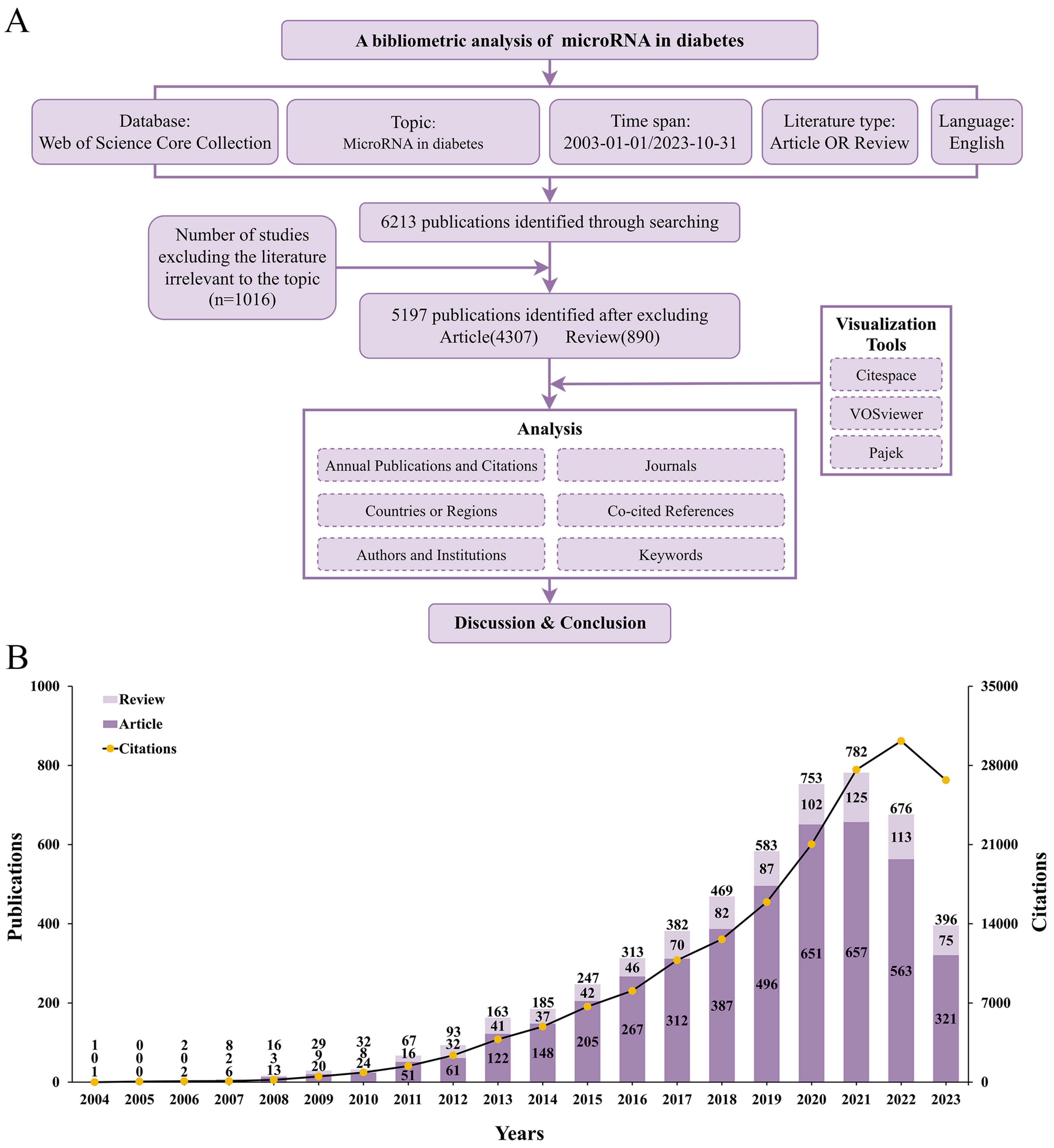


Figure 1 (A) Flowchart of bibliometric analysis. (B) The number of articles about microRNA in diabetes per year from 2003 to 2023.

## Data Analysis

VOSviewer (version 1.6.20(0), Leiden University, Leiden, Netherlands), CiteSpace (version 6.2. R5, Chaomei Chen, Drexel University, Philadelphia, PA, United States), Microsoft Excel 2019MSO (version2404 Build 16.0.17531.20140, 64bit), the R language based Bibliometrix Package (4.1.3 Package) and Scimago Graphica (Beta 1.0.36) were used to support our data analysis. VOSviewer was utilized to build and view the co-occurrence maps among countries/regions and the maps of co-occurrence and collaboration among institutions.[13] CiteSpace was applied to construct a keyword burst map and to analyze references.[14] The Bibliometric package (4.1.3 package) based on R language was used to analyze the relationships between co-cited authors, references, and keywords.

# Results

## Annual Publications and Citations

After excluding 1016 irrelevant studies manually, a total of 5197 papers were involved in our study, and the annual number of publications and citations were counted. As shown in Figure 1B, both the number of publications and citations increased steadily during the period we studied, and the growth has sped up since 2018. Annual publications reached their peak in 2021 (782 articles), while citations peaked the following year at 30,153 (Figure 1B). This growth trajectory revealed distinctive patterns: publications demonstrated remarkable expansion with an average annual growth rate of 45% from 2004–2021, accelerating to 29.2% during the 2018–2021 surge period. Similarly, citations maintained robust 58% average annual growth until 2022. Statistical modeling confirmed excellent fit for both patterns: we used cubic polynomial regression for publications ($R^2 = 0.9926$) and exponential regression for citations ($R^2 = 0.9813$). However, a significant reversal occurred in 2022–2023, with publications declining consecutively by 13.6% and 41.4%, and citations falling by 11.5%. This indicates that the field reached peak influence in 2021–2022, followed by a pronounced contraction. Despite this recent reversal, the sustained growth in engagement prior to 2022 was significant. In particular, the accelerated pace observed since 2018 underscores persistently escalating academic interest in microRNAs and diabetes leading up to the inflection point. This highlights the need for close monitoring of emerging trends within the field.

## Analysis of Cooperation Status

### Countries/Regions

A total of 86 countries have made contributions to the research of microRNA in diabetes. In Figure 2A, the top ten most productive countries were listed in the bar chart, with the longitudinal axis figuring out the number of publications respectively. The most productive country/region was China (n = 2796), followed by the United States (n = 935), Italy (n = 255), Iran (n = 213), and Germany (n = 180) (Figure 2A). The top 10 countries, constituting four Asian countries, three European countries, two American countries, and one country in Oceania, conjointly published 5081 literatures. Figure 2B displays the extensive cooperation between the most productive countries/regions. In this Figure, by limiting countries with a minimum number of papers of 20 or more, 33 countries met the requirement and were displayed on the chart (Figure 2B). Two notable clusters were shaped out of the 33 countries that held several over 900 articles, respectively. As depicted from the diameter of the circle, China demonstrated the largest proportion of publications among countries worldwide, with the United States approaching second. China's overwhelming output dominance highlights its strategic focus on this field. Also, the formation of two distinct high-volume collaboration clusters (each>900 publications) signals robust international research networks, though regional partnerships remain prevalent.

### Institutions

The research on microRNAs in diabetes was performed in a total of 4146 institutions worldwide. After purifying them, we got 70 institutions, belonging to 7 clusters. Table 1 shows the top 10 productive institutions by the number of literature outputs and citations. Nanjing Medical University had the most significant number of publications (148 publications, 4831 citations), showcasing itself as a main contributor to the output of this field. Closely followed by Central South University (130 publications, 4023 citations). Particularly, Shanghai Jiao Tong University excelled at holding the highest citations, considerably reaching 6903, which represented that the institution led a relatively high

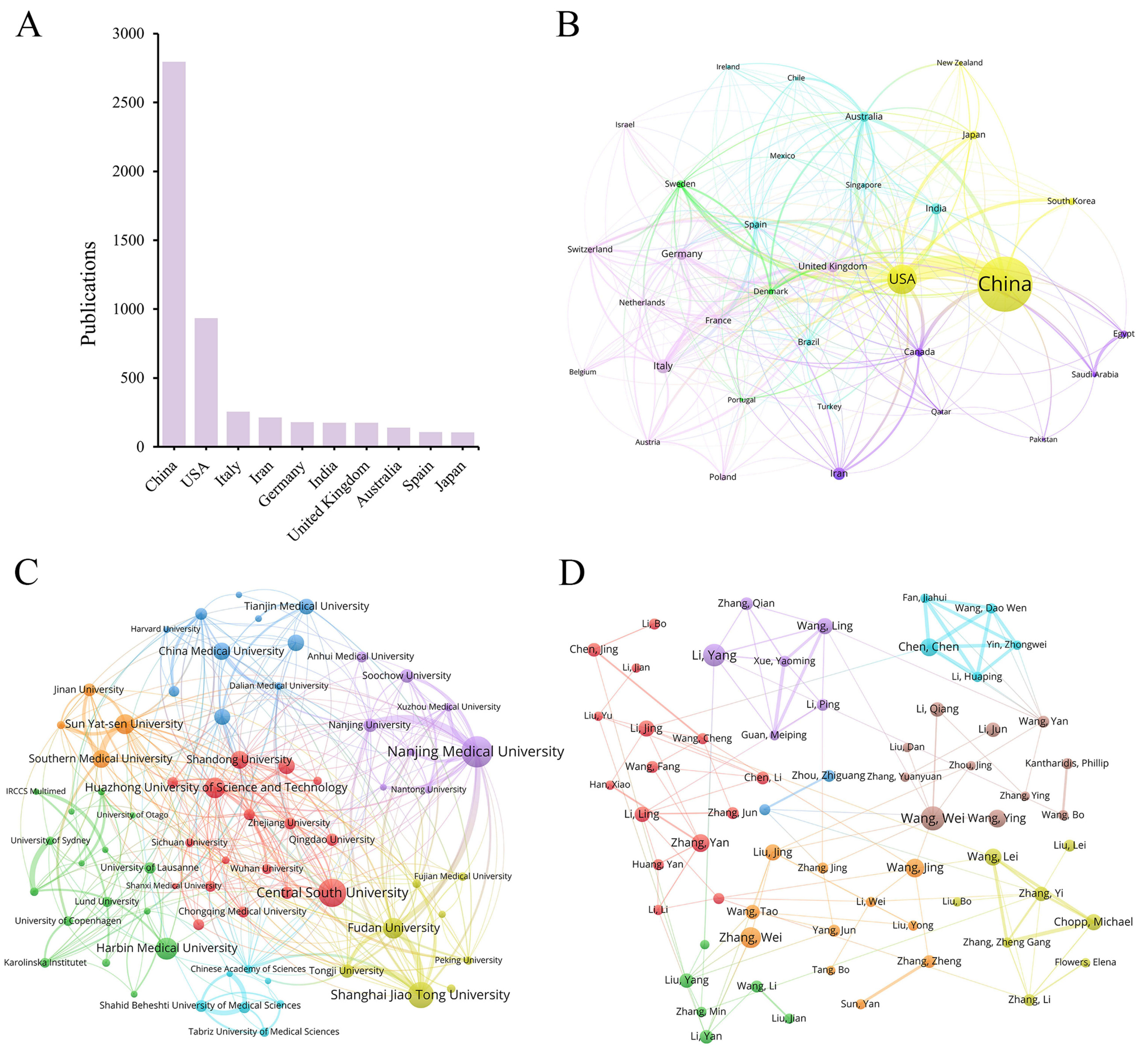


**Figure 2** (**A**) The top 10 productive countries/regions. The network maps showing countries/regions (**B**), institutions (**C**) and authors (**D**) involve in the research on microRNA in diabetes. Network maps based on dual-map overlays were constructed in VOSviewer.

quality in producing articles. Leading Chinese institutions drive both volume (Nanjing Medical) and high-impact research (Shanghai Jiao Tong). Moreover, Figure 2C demonstrates the primary institutions and their partnerships in this field, where a color closer to yellow indicates higher activity recently, whereas a color closer to blue signifies lower

**Table 1** The Top 10 Productive Institutions

| Institution | Publications | Citations |
|---|---|---|
| Nanjing Medical University | 148 | 4831 |
| Central South University | 130 | 4023 |
| Shanghai Jiao Tong University | 119 | 6903 |

(*Continued*)

**Table 1** (Continued).

| Institution | Publications | Citations |
|---|---|---|
| Harbin Medical University | 96 | 2724 |
| Fudan University | 89 | 4123 |
| Huazhong University of Science and Technology | 88 | 1927 |
| Sun Yat-sen University | 84 | 2517 |
| Shandong University | 74 | 1791 |
| Southern Medical University | 73 | 2225 |
| China Medical University | 71 | 1514 |

activity. The co-occurrence analysis of institutions also found that close cooperation existed among institutions with a large number of publications, and domestic cooperation was more common than international cooperation. The co-occurrence analysis revealing stronger domestic vs international collaboration suggests potential for more cross-border partnerships to accelerate discovery.

## Authors

24320 researchers participated in relative research, but only 64 researchers have published at least 10 articles and are in connection with others. The top 10 most prolific authors are shown in Table 2. Natarajan Rama (33 publications, 4342 total citations, 131.58 per citation) from the USA ranked first, followed by Regazzi Romano (32 publications, 3137 total citations, 98.03 per citation) from Switzerland. Notably, Kato Mitsuo (25 publications, 3428 total citations, 137.12 per citation) won the most citations per document, indicating his articles were of great reference value. Overall, key opinion leaders like Natarajan and Kato demonstrate exceptional influence, evidenced by high citation rates. In Figure 2D, the size of each node corresponds to the number of articles the author carried out. Authors in one cluster are considered to be collaborating relatively closer, and the cooperation frequency is represented by the thickness between nodes. The clear author clusters reflect established collaborative teams central to advancing this field.

**Table 2** The Top 10 Productive Authors

| Name | Country | Publications | Total citations | Per Citations |
|---|---|---|---|---|
| Natarajan, Rama | USA | 33 | 4342 | 131.58 |
| Regazzi, Romano | Switzerland | 32 | 3137 | 98.03 |
| Wang, Wei | China | 28 | 636 | 22.71 |
| Li, Yang | China | 26 | 854 | 32.85 |
| Kato, Mitsuo | USA | 25 | 3428 | 137.12 |
| Eliasson, Lena | Sweden | 24 | 1097 | 45.71 |
| Zhang, Wei | China | 24 | 638 | 26.58 |
| Dotta, Francesco | Italy | 21 | 882 | 42.00 |
| Wang, Jing | China | 21 | 694 | 33.05 |
| Chen, Chen | China | 20 | 605 | 30.25 |

**Table 3** The Top 10 Journals of Publications on microRNA in Diabetes (Sorted by Total Citations)

| Journal | Category | Impact Factor (2022) | Total Publications (%) | Total Citations |
|---|---|---|---|---|
| Diabetes | Endocrinology; Diabetes & Metabolism; Internal Medicine | 7.7 | 86 (1.66) | 7838 |
| PLOS ONE | Multidisciplinary | 3.7 | 118 (2.27) | 5412 |
| Circulation Research | Physiology; Cardiology & Cardiovascular Medicine | 20.1 | 19 (0.37) | 4856 |
| Scientific Reports | Multidisciplinary | 4.6 | 108 (2.08) | 4263 |
| Diabetologia | Endocrinology; Diabetes & Metabolism; Internal Medicine | 8.2 | 58 (1.12) | 3821 |
| International Journal of Molecular Sciences | Molecular Biology; Catalysis; Inorganic; Chemistry; Organic Chemistry; Physical & Theoretical Chemistry; Spectroscopy; Computer Science Applications; Medicine (miscellaneous) | 5.6 | 147 (2.83) | 3445 |
| Biochemical and Biophysical Research Communications | Biochemistry; Biophysics; Cell Biology; Molecular Biology | 3.1 | 88 (1.69) | 3384 |
| Nature | Multidisciplinary | 64.8 | 5 (0.10) | 3082 |
| Cell Research | Cell Biology; Molecular Biology | 44.1 | 1 (0.02) | 2984 |
| Journal of Cellular Physiology | Cell Biology; Clinical Biochemistry; Physiology | 5.6 | 60 (1.16) | 2523 |

## Analysis of Journals

Until October 2023, 1003 scientific journals have delivered publications on this topic. Table 3 reveals a rank of the top 10 journals, listed in order regarding the total number of citations they have collected, accounting for 23.73% of the whole. Diabetes (7.7 impact factor, 86 total publications), PLOS ONE (3.7 impact factor, 118 total publications), and Circulation Research (20.1 impact factor, 19 total publications) are the top three journals, with the total citations respectively reaching 7838, 5412, and 4856. The impact factor manifests the frequency of article citations. In particular, Nature stood out with the most impact factor (n = 64.8), which was supposed to be of the hit academic influence and great research value regarding the quality of its articles. Considering the following Cell Research (n = 44.1) and Circulation Research (n = 20.1), these three journals were the only three journals with an impact factor over 10. In general, publication in high-impact journals like Nature signals the field's growing recognition for fundamental discovery. The dual-map overlay of journals presented in Figure 3 illustrates the topic distribution of these journals, with the citing journals being positioned on the left side of the map and the cited journals on the right. As indicated on the left side of the map, the articles were

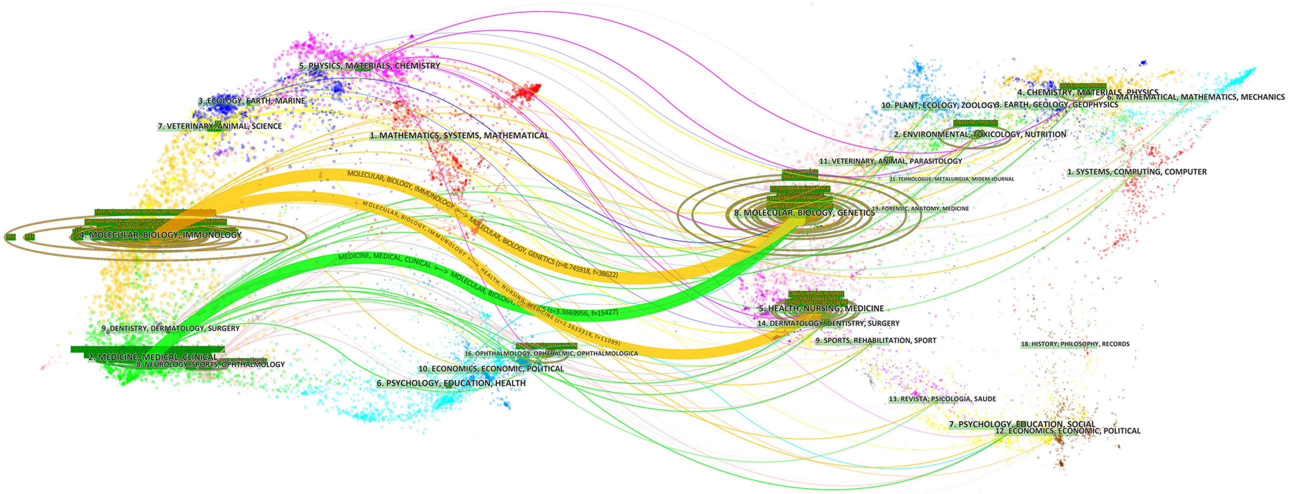


**Figure 3** The dual-map overlay of journals, with the distribution of journals of the citation of literature on the left, and the distribution of journals corresponding to the cited literature on the right. Dual overlay maps were generated by Citespace.

published in two disciplines ("molecular biology immunology" and "medicine medical clinical"). The yellow citation paths in the figure represent that the knowledge base of publications was mainly in the realms of "health nursing medicine" and "molecular biology genetics" in the past. Meanwhile, the green citation path reveals that the knowledge base in this realm was mostly in the discipline of "molecular biology genetics" lately. Substantially, the dual-map overlay confirms research spans molecular biology to clinical medicine, with knowledge foundations evolving towards "molecular biology/genetics".

## Analysis of Co-Cited References

CiteSpace was applied to carry out the co-citations of references by comparing lists of citing documents. Figure 4A illustrates the top 16 distribution networks of co-cited references from 2003 to 2023. The size of a node directly corresponds to its co-citation frequency. In Table 4, the top 10 co-cited references based on the number of co-citations were listed. Bartel et al's paper published in Cell is of the greatest number of co-citations, which is entitled "MicroRNAs: genomics, biogenesis, mechanism, and function" (n = 600), followed by his paper in European Heart Journal entitled "MicroRNAs: Target Recognition and Regulatory Functions" (n = 459).[15,16] Table 4 also shows that Zampetaki et al (2010),[17] Livak et al (2001),[18] and Poy et al (2004 and 2009)[19,20] ranked closely with Bartel et al (2004 and 2009) at the front, contributing a lot to the field of miRNAs in DM. Figure 4B showcases the 10 largest clusters as generated via the log-likelihood ratio (LLR) algorithm of CiteSpace. In the timeline view, nodes of different colors closer to the right indicate the latest references, which were sorted into clusters by their years via displaying them on several lines. The 10 largest clusters were labeled as 1) diabetic retinopathy, 2) diabetic nephropathy, 3) metabolic memory, 4) fibrosis, 5) insulin-like growth factor 2 receptor, 6) development, 7) rab, and 8) pancreatic beta-cell lines respectively. Containing 141 references, cluster 1) is the largest and most recent cluster.

The visual analysis of citation bursts of references reveals that the literature was more frequently cited in a short period, indicating that it was a hotspot of the time. In Figure 5, the top 50 with the strongest citation burst are listed, with the red bar indicating high citation frequency and fewer citations in blue. The paper entitled "Plasma microRNA profiling reveals loss of endothelial miR-126 and other microRNAs in type 2 diabetes" published by Zampetaki A. (2010)[17] received the strongest burst strength (50.76 strength, 2011–2015 burst period), followed by Obrien J. (2018) (42.7 strength, 2020–2023 burst period),[23] Guay C. (2013) (40.46 strength, 2015–2018 burst period),[24] and Bartel DP. (2009) (40.15 strength, 2010–2014 burst period).[16] Currently active citation bursts for ongoing research frontiers are systematically cataloged in Table 5, where references undergoing present-day citation surges are detailed.

In summary, Bartel's foundational work remains the cornerstone of miRNA research. Furthermore, the prominence of clinical clusters like diabetic retinopathy (#1) and nephropathy (#2) reflects the field's strong translational focus on diabetes complications. Current citation bursts (eg, Obrien J., 2020–2023) pinpoint active research frontiers.

## Analysis of Keywords

The co-occurring keywords that reflect the hotpots and the core contents of articles in the field were analyzed. In a total of 12620 keywords from 5197 papers retrieved, the top 100 most frequent keywords were extracted and clustered in Figure 6A, with each keyword appearing at least 83 times. In Figure 6A, four clusters of keywords are illustrated, each comprising 34, 29, 19, and 18 keywords respectively, with distinct colors to distinguish the clusters. Cluster 1 (red) includes keywords related to the factors affecting expressions of miRNAs, such as "inflammation", "mechanism", "oxidative stress", "apoptosis", "activation" and "disease". Cluster 2 (green) mainly focuses on the causative factors of DM. Keywords in this cluster include "microRNA", "diabetes", "insulin resistance", "gene expression", and "adipose tissue". Cluster 3 (blue) and Cluster 4 (yellow) focus on the role of miRNAs as biomarkers of DM-related diseases and the function of miRNAs mainly in diabetic nephropathy. The keywords with high citation frequency were revealed via the density view (Figure 6B). "MicroRNA", "expression", "insulin resistance", "diabetes", "diabetes mellitus", "apoptosis", "biomarker", "diabetic nephropathy", "cell", and "oxidative stress" are shown in high-density, indicating the focus of attention on miRNAs in DM. In Figure 6C, different colors were used to differentiate the keywords' occurring time. Keywords that appeared earlier are shown in white, whereas keywords that emerged more up-to-date are shown in dark purple. The latest keywords include "extracellular vesicles", "diabetic retinopathy", "pregnancy", "long noncoding RNA", "diabetic cardiomyopathy", and "diabetic kidney disease". The top 25 keywords with

**Figure 4** The collaboration of authors and co-cited references in the field of miRNAs in DM. (**A**) The figure only shows the top 16 authors' names. Cooperation networks with timeline overlays visualized collaborative dynamics among co-cited references in the studies of miRNAs in DM. (**B**) The largest 10 clusters of co-cited references (based on time clustering) in the studies of miRNAs in DM. Co-citation maps were created by Citspace.

the strongest citation bursts in the field of DM from 2004 to 2023 are shown in Figure 6D. "Long noncoding RNA", "gestational diabetes mellitus", "diabetic cardiomyopathy", "diabetic retinopathy", "apoptosis", "exosome", and "extracellular vesicles" are keywords that were still in a state of burst, suggesting the latent research hotspot in this field in the future. Especially, emerging keywords such as "exosomes" suggest a shift toward understanding intercellular miRNA signaling in DM.

https://doi.org/10.2147/JMDH.S533519

**Table 4** The Top 10 Co-Cited References

| First Author | Year | Journal | Title | Co-Citations |
|---|---|---|---|---|
| Bartel, et al | 2004 | Cell | MicroRNAs: genomics, biogenesis, mechanism, and function[15] | 600 |
| Bartel, et al | 2009 | European Heart Journal | MicroRNAs: Target Recognition and Regulatory Functions[16] | 459 |
| Zampetaki, et al | 2010 | Circulation Research | Plasma MicroRNA Profiling Reveals Loss of Endothelial MiR-126 and Other MicroRNAs in Type 2 Diabetes[17] | 426 |
| Livak, et al | 2001 | Methods | Analysis of Relative Gene Expression Data Using Real-Time Quantitative PCR and the $2^{-\Delta\Delta CT}$ Method[18] | 415 |
| Poy, et al | 2004 | Nature | A pancreatic islet-specific microRNA regulates insulin secretion[19] | 409 |
| Poy, et al | 2009 | Proceedings of the National Academy of Sciences of the United States of America | miR-375 maintains normal pancreatic α- and β-cell mass[20] | 265 |
| Kong, et al | 2010 | Acta Diabetologica | Significance of serum microRNAs in pre-diabetes and newly diagnosed type 2 diabetes: a clinical study[21] | 251 |
| Kato, et al | 2007 | Proceedings of the National Academy of Sciences of the United States of America | MicroRNA-192 in diabetic kidney glomeruli and its function in TGF-β-induced collagen expression via inhibition of E-box repressors | 226 |
| Ambros, et al | 2004 | Nature | The functions of animal microRNAs | 220 |
| Trajkovski, et al | 2011 | Nature | MicroRNAs 103 and 107 regulate insulin sensitivity[22] | 216 |

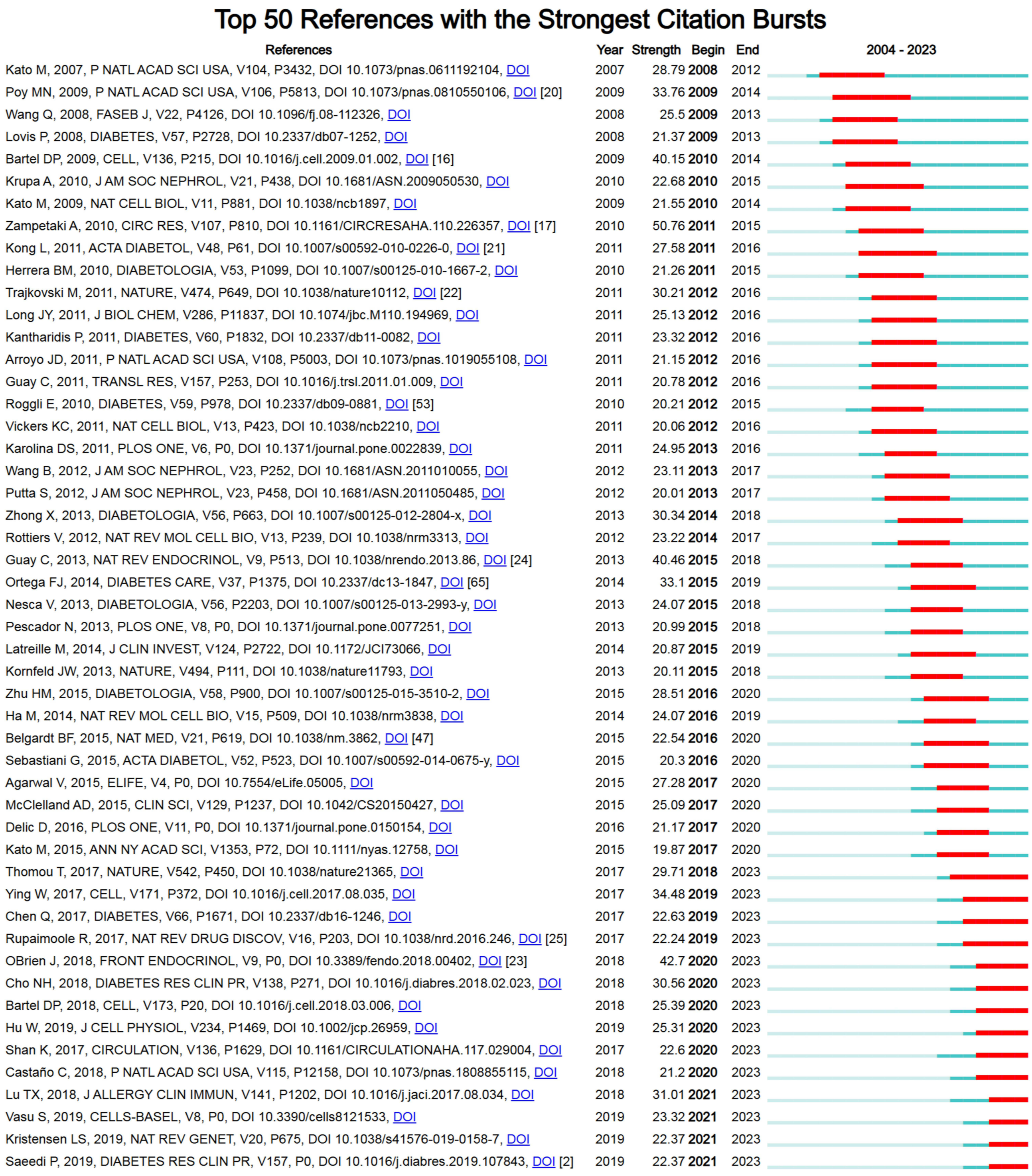
These clusters map the field's core themes: understanding molecular drivers, disease origins, and diagnostic/clinical applications. Burst keywords like "exosomes", "extracellular vesicles", and "diabetic cardiomyopathy" highlight critical emerging directions. The shift towards intercellular miRNA signaling (via exosomes/vesicles) and specific complications (retinopathy, cardiomyopathy, kidney disease) defines the current research vanguard.

# Discussion

MicroRNAs have been raised as a beacon of hope for DM patients. In our study, VOSviewer and CiteSpace were utilized to conduct a comprehensive bibliometric study, exploring the latest research developments, identifying significant research areas, and depicting future trends in the field of miRNAs in DM. 5917 publications indexed from 2003–2023 were included in the integrated study. Several relevant tables and figures were carried out by analyzing and presenting data on countries/regions, institutions, authors, references, and keywords relevant to our topic. Through careful analysis based on the WOSCC database, we aim to share a detailed investigation of research progress in this domain, hoping to catalyze the development of this field.

## Bibliometric Information

The study of microRNAs (miRNAs) has transformed our understanding of diabetes pathogenesis and therapeutics over the past three decades. This journey began in 1993 with the seminal discovery of lin-4 in C. elegans,[26–28] accelerated by Bartel et al's identification of let-7 as a conserved genetic regulator,[15] and gained metabolic relevance when Xu et al linked miR-14 to fat metabolism.[29] Poy et al then established miRNAs as critical modulators of insulin secretion,[19] paving the way for Gauthier et al's breakthrough demonstration that miRNAs govern insulin exocytosis—unlocking new therapeutic avenues for diabetes.[30] Fueled by the global surge in diabetes prevalence, mortality, and unmet clinical needs,[2,31,32] this field continues its exponential growth.



Top 50 References with the Strongest Citation Bursts

| References | Year | Strength | Begin | End |
|---|---|---|---|---|
| Kato M, 2007, P NATL ACAD SCI USA, V104, P3432, DOI 10.1073/pnas.0611192104, DOI | 2007 | 28.79 | **2008** | 2012 |
| Poy MN, 2009, P NATL ACAD SCI USA, V106, P5813, DOI 10.1073/pnas.0810550106, DOI [20] | 2009 | 33.76 | **2009** | 2014 |
| Wang Q, 2008, FASEB J, V22, P4126, DOI 10.1096/fj.08-112326, DOI | 2008 | 25.5 | **2009** | 2013 |
| Lovis P, 2008, DIABETES, V57, P2728, DOI 10.2337/db07-1252, DOI | 2008 | 21.37 | **2009** | 2013 |
| Bartel DP, 2009, CELL, V136, P215, DOI 10.1016/j.cell.2009.01.002, DOI [16] | 2009 | 40.15 | **2010** | 2014 |
| Krupa A, 2010, J AM SOC NEPHROL, V21, P438, DOI 10.1681/ASN.2009050530, DOI | 2010 | 22.68 | **2010** | 2015 |
| Kato M, 2009, NAT CELL BIOL, V11, P881, DOI 10.1038/ncb1897, DOI | 2009 | 21.55 | **2010** | 2014 |
| Zampetaki A, 2010, CIRC RES, V107, P810, DOI 10.1161/CIRCRESAHA.110.226357, DOI [17] | 2010 | 50.76 | **2011** | 2015 |
| Kong L, 2011, ACTA DIABETOL, V48, P61, DOI 10.1007/s00592-010-0226-0, DOI [21] | 2011 | 27.58 | **2011** | 2016 |
| Herrera BM, 2010, DIABETOLOGIA, V53, P1099, DOI 10.1007/s00125-010-1667-2, DOI | 2010 | 21.26 | **2011** | 2015 |
| Trajkovski M, 2011, NATURE, V474, P649, DOI 10.1038/nature10112, DOI [22] | 2011 | 30.21 | **2012** | 2016 |
| Long JY, 2011, J BIOL CHEM, V286, P11837, DOI 10.1074/jbc.M110.194969, DOI | 2011 | 25.13 | **2012** | 2016 |
| Kantharidis P, 2011, DIABETES, V60, P1832, DOI 10.2337/db11-0082, DOI | 2011 | 23.32 | **2012** | 2016 |
| Arroyo JD, 2011, P NATL ACAD SCI USA, V108, P5003, DOI 10.1073/pnas.1019055108, DOI | 2011 | 21.15 | **2012** | 2016 |
| Guay C, 2011, TRANSL RES, V157, P253, DOI 10.1016/j.trsl.2011.01.009, DOI | 2011 | 20.78 | **2012** | 2016 |
| Roggli E, 2010, DIABETES, V59, P978, DOI 10.2337/db09-0881, DOI [53] | 2010 | 20.21 | **2012** | 2015 |
| Vickers KC, 2011, NAT CELL BIOL, V13, P423, DOI 10.1038/ncb2210, DOI | 2011 | 20.06 | **2012** | 2016 |
| Karolina DS, 2011, PLOS ONE, V6, P0, DOI 10.1371/journal.pone.0022839, DOI | 2011 | 24.95 | **2013** | 2016 |
| Wang B, 2012, J AM SOC NEPHROL, V23, P252, DOI 10.1681/ASN.2011010055, DOI | 2012 | 23.11 | **2013** | 2017 |
| Putta S, 2012, J AM SOC NEPHROL, V23, P458, DOI 10.1681/ASN.2011050485, DOI | 2012 | 20.01 | **2013** | 2017 |
| Zhong X, 2013, DIABETOLOGIA, V56, P663, DOI 10.1007/s00125-012-2804-x, DOI | 2013 | 30.34 | **2014** | 2018 |
| Rottiers V, 2012, NAT REV MOL CELL BIO, V13, P239, DOI 10.1038/nrm3313, DOI | 2012 | 23.22 | **2014** | 2017 |
| Guay C, 2013, NAT REV ENDOCRINOL, V9, P513, DOI 10.1038/nrendo.2013.86, DOI [24] | 2013 | 40.46 | **2015** | 2018 |
| Ortega FJ, 2014, DIABETES CARE, V37, P1375, DOI 10.2337/dc13-1847, DOI [65] | 2014 | 33.1 | **2015** | 2019 |
| Nesca V, 2013, DIABETOLOGIA, V56, P2203, DOI 10.1007/s00125-013-2993-y, DOI | 2013 | 24.07 | **2015** | 2018 |
| Pescador N, 2013, PLOS ONE, V8, P0, DOI 10.1371/journal.pone.0077251, DOI | 2013 | 20.99 | **2015** | 2018 |
| Latreille M, 2014, J CLIN INVEST, V124, P2722, DOI 10.1172/JCI73066, DOI | 2014 | 20.87 | **2015** | 2019 |
| Kornfeld JW, 2013, NATURE, V494, P111, DOI 10.1038/nature11793, DOI | 2013 | 20.11 | **2015** | 2018 |
| Zhu HM, 2015, DIABETOLOGIA, V58, P900, DOI 10.1007/s00125-015-3510-2, DOI | 2015 | 28.51 | **2016** | 2020 |
| Ha M, 2014, NAT REV MOL CELL BIO, V15, P509, DOI 10.1038/nrm3838, DOI | 2014 | 24.07 | **2016** | 2019 |
| Belgardt BF, 2015, NAT MED, V21, P619, DOI 10.1038/nm.3862, DOI [47] | 2015 | 22.54 | **2016** | 2020 |
| Sebastiani G, 2015, ACTA DIABETOL, V52, P523, DOI 10.1007/s00592-014-0675-y, DOI | 2015 | 20.3 | **2016** | 2020 |
| Agarwal V, 2015, ELIFE, V4, P0, DOI 10.7554/eLife.05005, DOI | 2015 | 27.28 | **2017** | 2020 |
| McClelland AD, 2015, CLIN SCI, V129, P1237, DOI 10.1042/CS20150427, DOI | 2015 | 25.09 | **2017** | 2020 |
| Delic D, 2016, PLOS ONE, V11, P0, DOI 10.1371/journal.pone.0150154, DOI | 2016 | 21.17 | **2017** | 2020 |
| Kato M, 2015, ANN NY ACAD SCI, V1353, P72, DOI 10.1111/nyas.12758, DOI | 2015 | 19.87 | **2017** | 2020 |
| Thomou T, 2017, NATURE, V542, P450, DOI 10.1038/nature21365, DOI | 2017 | 29.71 | **2018** | 2023 |
| Ying W, 2017, CELL, V171, P372, DOI 10.1016/j.cell.2017.08.035, DOI | 2017 | 34.48 | **2019** | 2023 |
| Chen Q, 2017, DIABETES, V66, P1671, DOI 10.2337/db16-1246, DOI | 2017 | 22.63 | **2019** | 2023 |
| Rupaimoole R, 2017, NAT REV DRUG DISCOV, V16, P203, DOI 10.1038/nrd.2016.246, DOI [25] | 2017 | 22.24 | **2019** | 2023 |
| OBrien J, 2018, FRONT ENDOCRINOL, V9, P0, DOI 10.3389/fendo.2018.00402, DOI [23] | 2018 | 42.7 | **2020** | 2023 |
| Cho NH, 2018, DIABETES RES CLIN PR, V138, P271, DOI 10.1016/j.diabres.2018.02.023, DOI | 2018 | 30.56 | **2020** | 2023 |
| Bartel DP, 2018, CELL, V173, P20, DOI 10.1016/j.cell.2018.03.006, DOI | 2018 | 25.39 | **2020** | 2023 |
| Hu W, 2019, J CELL PHYSIOL, V234, P1469, DOI 10.1002/jcp.26959, DOI | 2019 | 25.31 | **2020** | 2023 |
| Shan K, 2017, CIRCULATION, V136, P1629, DOI 10.1161/CIRCULATIONAHA.117.029004, DOI | 2017 | 22.6 | **2020** | 2023 |
| Castaño C, 2018, P NATL ACAD SCI USA, V115, P12158, DOI 10.1073/pnas.1808855115, DOI | 2018 | 21.2 | **2020** | 2023 |
| Lu TX, 2018, J ALLERGY CLIN IMMUN, V141, P1202, DOI 10.1016/j.jaci.2017.08.034, DOI | 2018 | 31.01 | **2021** | 2023 |
| Vasu S, 2019, CELLS-BASEL, V8, P0, DOI 10.3390/cells8121533, DOI | 2019 | 23.32 | **2021** | 2023 |
| Kristensen LS, 2019, NAT REV GENET, V20, P675, DOI 10.1038/s41576-019-0158-7, DOI | 2019 | 22.37 | **2021** | 2023 |
| Saeedi P, 2019, DIABETES RES CLIN PR, V157, P0, DOI 10.1016/j.diabres.2019.107843, DOI [2] | 2019 | 22.37 | **2021** | 2023 |

**Figure 5** The top 50 references with the strongest citation bursts, based on CiteSpace, that were involved in miRNAs in DM between 2004 and 2023. The blue line represents the time from its first appearance to 2023, and the red line represents the burst time.

Bibliometric trends reflect this dynamism (Figure 1B). Publication output peaked in 2021, while citations crested in 2022. The 2019–2021 period saw increased article and review volumes, though the COVID-19 pandemic likely disrupted experimental studies, contributing to a 2022 publication decline. Despite a modest citation dip in 2023 (attributable to data collection timing), projections indicate renewed growth—contrasting sharply with WHO's unfulfilled 2025 diabetes containment targets[28] and reinforcing the field's strategic importance.[29]

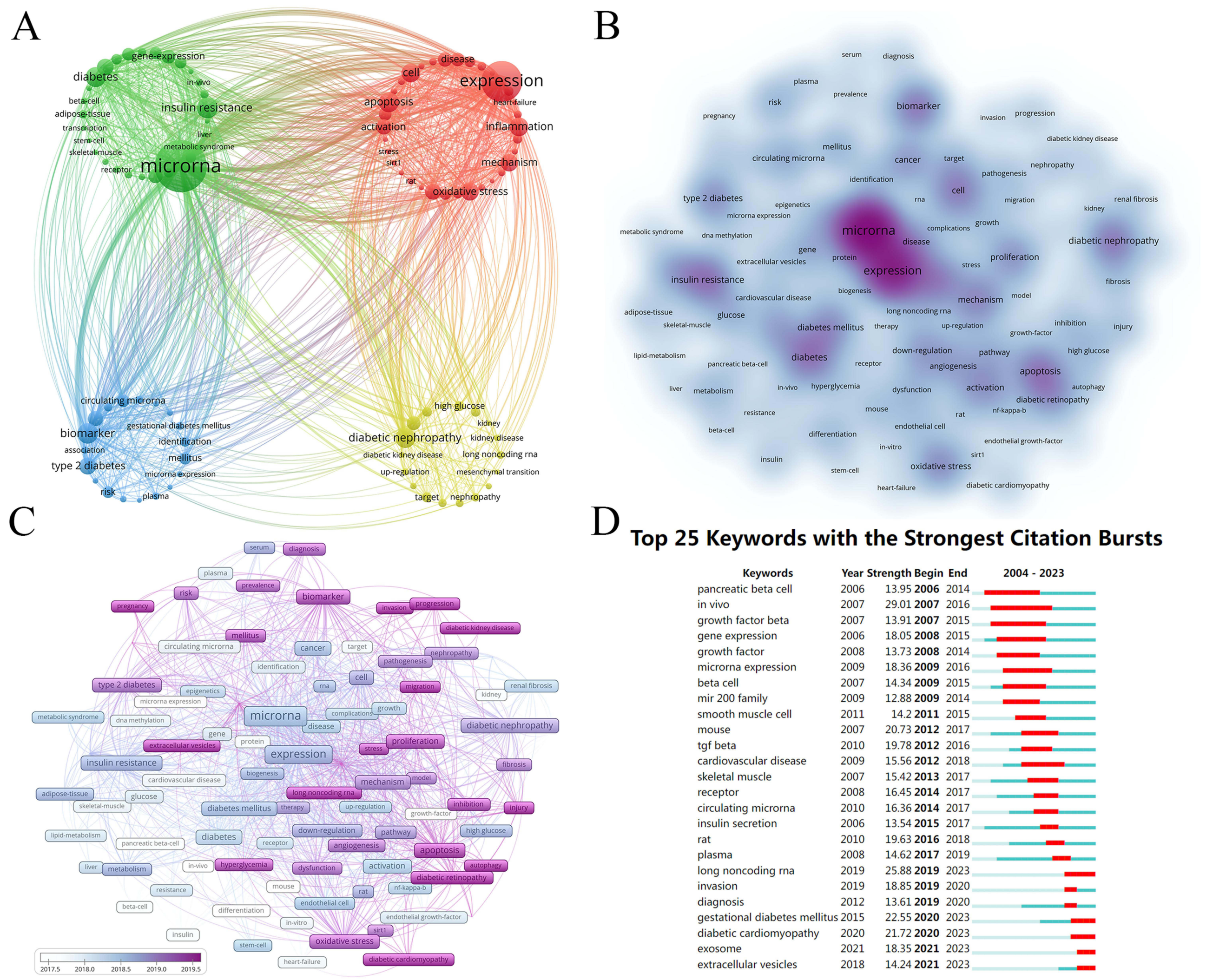
**Table 5** References Currently in a State of Burst

| Burst Period | First Author | Year | Journal | Title |
|---|---|---|---|---|
| 2018-2023 | Thomou, et al | 2017 | Nature | Adipose-derived circulating miRNAs regulate gene expression in other tissues |
| 2019-2023 | Ying, et al | 2017 | Cell | Adipose Tissue Macrophage-Derived Exosomal miRNAs Can Modulate In Vivo and In Vitro Insulin Sensitivity |
| 2019-2023 | Chen, et al | 2017 | Diabetes | Pathogenic Role of microRNA-21 in Diabetic Retinopathy Through Downregulation of PPARα |
| 2019-2023 | Rupaimoole, et al | 2017 | Nature Reviews Drug Discovery | MicroRNA therapeutics: towards a new era for the management of cancer and other diseases[25] |
| 2020-2023 | O'Brien, et al | 2018 | Frontiers in Endocrinology | Overview of MicroRNA Biogenesis, Mechanisms of Actions, and Circulation[23] |
| 2020-2023 | Cho, et al | 2018 | Diabetes Research and Clinical Practice | IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045 |
| 2020-2023 | Bartel, et al | 2018 | Cell | Metazoan MicroRNAs |
| 2020-2023 | Hu, et al | 2019 | Journal Cellular Physiology | Circular RNA circRNA_15698 aggravates the extracellular matrix of diabetic nephropathy mesangial cells via miR-185/TGF-β1 |
| 2020-2023 | Shan, et al | 2017 | Circulation | Circular Noncoding RNA HIPK3 Mediates Retinal Vascular Dysfunction in Diabetes Mellitus |
| 2020-2023 | Castaño, et al | 2019 | Proceedings of the National Academy of Sciences of the United States of America | Obesity-associated exosomal miRNAs modulate glucose and lipid metabolism in mice |
| 2020-2023 | Lu, et al | 2018 | Journal of Allergy and Clinical Immunology | MicroRNA |
| 2021-2023 | Vasu, et al | 2019 | Cells | MicroRNA Signatures as Future Biomarkers for Diagnosis of Diabetes States |
| 2021-2023 | Kristensen, et al | 2019 | Nature Reviews Genetics | The biogenesis, biology and characterization of circular RNAs |
| 2021-2023 | Saeedi, et al | 2019 | Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition | Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition[2] |

Geographically, China dominates contemporary research output (Figure 2), accounting for all top 10 productive institutions (Table 1), which is a response to its severe diabetes burden.[32–35] Yet citation analysis reveals nuanced gaps: only one Chinese study ranks among the top 10 co-cited references (Table 4), and China contributes just a single review to the most-cited articles (Table 6), signaling opportunities to enhance foundational research. Consequently, China has intensified collaborations, notably with the US (Figure 2B) and multinational consortia (Figure 2C), aiming to bridge this innovation gap.

Crucially, transformative contributions extend beyond high-output nations: O'Brien (Canada) detailed miRNA-mediated gene regulation via mRNA stability control and TLR (toll-like receptors) -driven intercellular communication;[23] Trajkovski (Switzerland) identified miR-103/107 inactivation as a therapeutic lever to boost insulin sensitivity through Caveolin-1;[22] Guay and Regazzi (Switzerland) validated circulating miRNAs as diabetes biomarkers;[24] Eliasson et al (multinational) uncovered miR-184 silencing in diabetic patients and its role in β-cell adaptation via Argonaute2 targeting.[37]

Collectively, these trends confirm miRNA-diabetes research is in a phase of vigorous, sustained expansion. As global collaborations mature and mechanistic insights deepen, this field holds exceptional promise for delivering novel strategies to alleviate the growing diabetes burden worldwide.



Top 25 Keywords with the Strongest Citation Bursts

| Keywords | Year | Strength | Begin | End |
|---|---|---|---|---|
| pancreatic beta cell | 2006 | 13.95 | **2006** | 2014 |
| in vivo | 2007 | 29.01 | **2007** | 2016 |
| growth factor beta | 2007 | 13.91 | **2007** | 2015 |
| gene expression | 2006 | 18.05 | **2008** | 2015 |
| growth factor | 2008 | 13.73 | **2008** | 2014 |
| microrna expression | 2009 | 18.36 | **2009** | 2016 |
| beta cell | 2007 | 14.34 | **2009** | 2015 |
| mir 200 family | 2009 | 12.88 | **2009** | 2014 |
| smooth muscle cell | 2011 | 14.2 | **2011** | 2015 |
| mouse | 2007 | 20.73 | **2012** | 2017 |
| tgf beta | 2010 | 19.78 | **2012** | 2016 |
| cardiovascular disease | 2009 | 15.56 | **2012** | 2018 |
| skeletal muscle | 2007 | 15.42 | **2013** | 2017 |
| receptor | 2008 | 16.45 | **2014** | 2017 |
| circulating microrna | 2010 | 16.36 | **2014** | 2017 |
| insulin secretion | 2006 | 13.54 | **2015** | 2017 |
| rat | 2010 | 19.63 | **2016** | 2018 |
| plasma | 2008 | 14.62 | **2017** | 2019 |
| long noncoding rna | 2019 | 25.88 | **2019** | 2023 |
| invasion | 2019 | 18.85 | **2019** | 2020 |
| diagnosis | 2012 | 13.61 | **2019** | 2020 |
| gestational diabetes mellitus | 2015 | 22.55 | **2020** | 2023 |
| diabetic cardiomyopathy | 2020 | 21.72 | **2020** | 2023 |
| exosome | 2021 | 18.35 | **2021** | 2023 |
| extracellular vesicles | 2018 | 14.24 | **2021** | 2023 |

**Figure 6** Keyword-related mapping in studies in the field of miRNAs in DM. (**A**) The figure only shows the top 25 keywords. Network map of the keywords created by VOSviewer in the studies of miRNAs in DM. (**B**) Subcategories of the main keywords that were utilized in the studies related to miRNAs in DM. Density plots created by VOSviewer. (**C**) A timeline view of keywords based on VOSviewe was generated to map the temporal overlay of research hotspots in the studies of miRNAs in DM, visualizing how thematic clusters evolved across distinct time periods. (**D**) The top 25 keywords with the strongest citation bursts by CiteSpace.

## Detection of Research Hotspots and Future Directions

### The Molecular Mechanisms of the Role of miRNAs

Deciphering the molecular mechanisms of miRNAs reveals their multifaceted roles in diabetes pathogenesis. Firstly, numerous studies highlight the critical roles of individual miRNAs in modulating insulin sensitivity, glucose metabolism,

**Table 6** The Top 10 Most Cited Articles

| Title | First Author | Journal | Year | Total Citations | Citations per Year |
|---|---|---|---|---|---|
| Characterization of microRNAs in serum: a novel class of biomarkers for diagnosis of cancer and other diseases | Chen, et al, | Cell Research | 2008 | 2984 | 175.53 |
| A pancreatic islet-specific microRNA regulates insulin secretion[19] | Poy, et al, | Nature | 2004 | 1687 | 80.33 |

(*Continued*)

https://doi.org/10.2147/JMDH.S533519

**Table 6** (Continued).

| Title | First Author | Journal | Year | Total Citations | Citations per Year |
|---|---|---|---|---|---|
| Plasma MicroRNA Profiling Reveals Loss of Endothelial MiR-126 and Other MicroRNAs in Type 2 Diabetes[17] | Zampetaki, et al, | Circulation Research | 2010 | 1141 | 76.07 |
| Diabetic Cardiomyopathy: An Update of Mechanisms Contributing to This Clinical Entity | Jia, et al, | Circulation Research | 2018 | 941 | 134.43 |
| Influence of cytochrome P450 polymorphisms on drug therapies: Pharmacogenetic, pharmacoepigenetic and clinical aspects | Ingelman-Sundberg, et al, | Pharmacology & Therapeutics | 2007 | 834 | 46.33 |
| Circulating MicroRNAs Novel Biomarkers and Extracellular Communicators in Cardiovascular Disease? | Creemers, et al, | Circulation Research | 2012 | 811 | 62.38 |
| MicroRNAs 103 and 107 regulate insulin sensitivity[22] | Trajkovski, et al, | Nature | 2011 | 782 | 55.86 |
| The Lin28/let-7 Axis Regulates Glucose Metabolism[36] | Zhu, et al, | Cell | 2011 | 702 | 50.14 |
| Circular RNAs are miRNA sponges and can be used as a new class of biomarker | Kulcheski, et al, | Journal of Biotechnology | 2016 | 608 | 67.56 |
| miR-375 maintains normal pancreatic α- and β-cell mass[20] | Poy, et al, | Proceedings of the National Academy of Sciences of the United States of America | 2009 | 603 | 37.69 |

and cellular stress responses. For instance, inactivation of miR-103/107 enhances insulin signaling via Caveolin-1 upregulation.[22] MiR-27a contributes to insulin resistance by targeting PPARγ.[38,39] MiR-21 overexpression improves hepatic insulin sensitivity by reducing FOXO1 levels,[40] while also protecting endothelial cells against high glucose-induced damage, potentially by inhibiting DAXX expression.[41] The expression of miR-21 is also regulated by various regulatory proteins, such as post-transcriptional TGF-β receptor (TGF-βR), phosphatase and tensin homolog (PTEN), and Smad7.[42] Conversely, miR-146a can inhibit Src phosphorylation and downstream targets VE-cadherin and Caveolin-1 to alleviate oxidative stress, which is supposed to be a promising therapeutic method for endothelial cell injury in DM.[43] MiR-192 targets E-cadherin and downregulates E-cadherin, leading to renal tubular cell fibrosis, and then causing diabetes nephropathy.[44] These findings underscore the direct regulatory impact of specific miRNAs on key pathways involved in metabolic homeostasis and cellular integrity in diabetes.

Secondly, miRNAs exert significant influence through their modulation of major signaling cascades implicated in DM pathophysiology. The insulin-PI3K-mTOR pathway, fundamental to growth and glucose metabolism, is regulated by miRNAs like let-7, which can impair glucose tolerance by inhibiting components like INSR and IRS2.[36] Within this pathway, PI3K/AKT and mTOR signaling regulate GLUT4 translocation; variations in miRNAs like miR-96 and miR-23a, associated with T2DM risk, may act through GLUT4-related pathways.[42,45] Other pathways are also targeted: miR-1249-3p regulates glucose homeostasis via the TLR4/NF-κB;[46] the miR-200 family contributes to β-cell apoptosis linked to Bax and Trp53 activation;[47,48] miR-223 activates the Keap1-Nrf2 system to combat oxidative stress.[49] Dysregulation of the NF-κB-miR-146a feedback loop has been implicated in diabetic neuropathy,[50] while the Sirt1/NF-κB/microR-29/Keap1 axis mediates renal tubular injury in nephropathy.[51] Furthermore, the TGF-β1-NF-κB-miR-21 pathway represents a potential therapeutic target for diabetic ulcers.[52] This extensive evidence demonstrates that miRNAs are integral regulators of complex signaling networks driving diabetic complications across multiple tissues.

Thirdly, beyond direct pathway modulation, miRNAs control cellular fate and function by fine-tuning gene expression, particularly influencing apoptotic processes relevant to β-cell loss and tissue damage. MiR-34a overexpression reduces insulin content and mRNA levels,[53] and induces β-cell apoptosis, potentially by targeting the 3'-UTR of Bcl-2.[47] MiR-21 knockdown promotes apoptosis in β-cells, suggesting its role in suppressing programmed cell death.[54–56] MiR-200a triggers β-cell apoptosis by targeting genes like XIAP.[47] In the context of nephropathy, miR-21 appears protective against podocyte loss by inhibiting pro-apoptotic signaling modulated by TGF-β/Smad3.[57] Conversely, nuclear miR-320 promotes cardiac lipotoxicity and dysfunction in diabetes by increasing CD36 expression.[58] These regulatory effects on gene expression, particularly concerning apoptosis regulators, highlight another crucial mechanism by which miRNAs contribute to the cellular dysfunction characteristic of diabetes.

## Applications of miRNAs in DM

MiRNA is a cluster of endogenous non-coding RNAs that regulates gene expression through its changes in expression, leading to diversification in the gene profile involved in a range of biological processes that result in many human diseases. The unique properties of miRNAs, particularly their stability in biofluids and disease/tissue-specific expression patterns, position them as highly promising tools for diagnosis, prognosis, and therapeutic intervention in diabetes.[59,60]

Numerous studies identify specific circulating miRNA profiles associated with different types and stages of diabetes, offering potential for non-invasive diagnosis and risk assessment. Altered levels of specific miRNAs (eg, downregulated miR-16-5p, miR-574-5p, miR-302d-3p; upregulated miR-25-3p) are reported in T1DM,[61] with distinct exosomal miRNAs (miR-122-5p, miR-193b-5p, miR-445-5p) distinguishing disease duration.[62] For T2DM/prediabetes, signatures including let-7a, let-7f, miR-326,[63] miR-15b, miR-486, miR-146b (in children),[64] clusters involving miR-30d, miR-9, miR-34a, miR-29a, miR-124a, miR-146a, miR-375,[21] miR-195, miR-423-5p, miR-126, miR-140-5p,[65] miR-375, miR-15a, miR-30a-5p, miR-150,[66] and miR-130a-3p, miR-1271-5p, miR-130p-3p, miR-574-3p[67] show diagnostic or predictive value. Changes in miRNAs like miR-146a, miR-24, miR-30d are also linked to insulin resistance pathways,[68] and broader miRNA panels are associated with β-cell function and glycemic control across the diabetes spectrum.[69] Importantly, circulating miR-193b and miR-192 may specifically mark prediabetes,[70] while miR-7, miR-192, and miR-152 show responsiveness to preventive interventions like Vitamin D.[71,72] Collectively, these findings strongly support the utility of miRNA signatures as sensitive biomarkers for detecting diabetes, distinguishing its subtypes, identifying high-risk individuals (prediabetes), and potentially monitoring responses to preventive measures.

Furthermore, miRNA dysregulation is also characteristic of specific diabetic complications, suggesting their use as biomarkers for early detection and progression monitoring. Reduced miR-590-3p is linked to diabetic nephropathy (DN),[73] with urine miRNAs showing high potential for monitoring early DN progression.[74] Specific urinary exosomal miRNA profiles (eg, upregulated miR-760, miR-188-5p, etc.; downregulated miR-153-3p, miR-133a-3p)[75] and circulating miRNAs like miR-342, miR-133b, miR-30,[76] and miR-4534[77] have been associated with DN. Glomerular miR-21 expression correlates with albuminuria in DN.[57] Circulating miR-21 is also proposed as a biomarker for diabetic cardiomyopathy (DCM).[78] Exosomal miR-210 and miR-15a are implicated in diabetic retinopathy (DR).[79,80] Altered miRNA responses (miR-143-3p, miR-191-5p, let-7b-5p, let-77g-5p) are observed in T2DM patients experiencing hypoglycemia.[81] Increased miR-21 in endothelial progenitor cells[41] and elevated miR-210[82] or distinct exosomal miR-24-3p expression[83] are reported in diabetic foot ulcers (DFU). These complication-specific miRNA alterations highlight their potential as valuable biomarkers for the early detection and monitoring of the diverse micro- and macrovascular complications arising from diabetes.

What's more, beyond diagnostics, miRNAs themselves represent attractive targets for novel therapeutic strategies in diabetes. Evidence suggests modulating specific miRNAs can improve metabolic parameters: miR-26a regulates insulin signaling and metabolism, suggesting therapeutic potential;[84] miR-21 overexpression enhances hepatic insulin sensitivity.[40] Pharmacological agents are also found to exert effects via miRNAs: sildenafil influences miR-22-3p/SIRT1 to improve adipose inflammation;[85] pioglitazone decreases hyperplasia via miR-24 upregulation[86] and alters EV miRNA profiles;[87] baseline miR-29c-3p and miR-145-5p levels predict response to insulin therapy;[88] exercise modulates miRNAs like miR-451a linked to metabolic pathways;[89] butyrate supplementation alters miR-9-5p and miR-146a-5p expression;[90] δ-tocotrienol improves glycemic control by regulating miR-34a, miR-375, miR-21, miR-132, miR-126;[91] astaxanthin downregulates miR-146a;[92] different antidiabetic drugs (glimepiride vs liraglutide) differentially affect plasma miRNAs (miR-206, miR-182-5p, miR-766-3p);[93] tadalafil modulates the miR-199-5p/α-Klotho axis to reduce inflammation in diabetic kidney disease.[94] These studies demonstrate the feasibility of targeting specific miRNAs either directly or indirectly through existing or novel therapeutics, opening avenues for developing miRNA-based diabetes treatments.

In addition, direct therapeutic application of miRNAs or miRNA inhibitors is actively being explored, though clinical translation in diabetes is still nascent. While miRNA therapeutics are advancing in other fields like cancer,[95] clinical application in diabetes is limited. Currently, antimiR-103/107 (RG-125/AZD4076) is in Phase I/IIa trials for T2DM and NAFLD.[22] Promising preclinical strategies include: EV-miRNAs as potential delivery vehicles or therapeutics;[9] miR-590-3p targeting CX3CL1 in DN;[73] MSC-derived exosomes (MSC-Exos) carrying therapeutic ncRNAs (eg, miR-486-3p, miR-126 for DR via TLR4/NF-κB and HMGB1 pathways;[96] miR-16-5p for DN protecting podocytes and inhibiting VEGFA;[97] miR-125b inducing autophagy via TRAF6/Akt axis in DN;[97] M2 macrophage-derived exosomal miR-25-3p improving podocyte injury in DN)[98] Preclinical studies offer significant promise for miRNA-based therapies targeting diabetic complications, particularly using engineered EVs. However, challenges like delivery efficiency and off-target effects[99–101] need resolution before widespread clinical use.

Overall, the compelling body of evidence confirms the strong association of miRNAs with diabetes onset and progression.[9,25] Their high feasibility as diagnostic and prognostic biomarkers is well-established across DM types and complications.[10,11,72,78] While establishing consensus on specific miRNA biomarker panels remains a current focus, the potential for miRNA-based therapeutics is increasingly tangible. The identification of numerous DM-relevant miRNAs[95,100,102–110] and the progress of miRNA targeting in other clinical areas provide a strong foundation. Nevertheless, significant challenges in specificity, delivery, and safety must be overcome before miRNA biomarkers and therapeutics achieve widespread clinical implementation for diabetes management.[111]

## Limitations

In this study, data from WOSCC were collected via a retrieval strategy and analyzed carefully. Nonetheless, some common limitations to bibliometric analysis also inevitably arose in our work. Firstly, our retrieval method of data inevitably included articles that did not fit our topic. To address the issue, we verified the records we found multiple times, screening each publication manually. Secondly, our bibliometric analysis, which exclusively depends on data from a single database, constrained the horizon of our findings. Thirdly, there are still some challenges and difficulties to overcome before miRNA is widely used as a biomarker for the clinical diagnosis or as a therapy for DM and its complications,[111] including off target of miRNAs,[112] specific delivery methods of miRNAs[9] (eg exosomal miRNAs), and ethic variations in miRNAs.[113] Fascinatingly, Sun W. et al declaimed that ultrasound facilitates exosome-mediated delivery of tissue-targeting mRNAs activated by miR-148a, enhancing therapeutic efficacy while minimizing off-target effects.[114] Moreover, due to the time constraints of our literature search, our research mainly focused on analyzing and describing the current state and temporal dynamics in the realm of miRNAs systematically. Hence, it was inevitable that we excluded some of the latest published articles from our research scope, some qualitative analyses were not performed, and the final results should be illuminated.

In order to explore the latest trends and key areas of interest of miRNA in DM, future research should include corresponding bibliometric analysis. Nevertheless, this bibliometric study conducted a detailed analysis and thorough examination of the literature data, providing valuable insights into the progress of miRNA in diabetes. It also emphasizes the prospects for future development and research hotspots in this field.

## Conclusions

Apparently, miRNAs have been considered to play a meritorious role in DM in recent years. The synthesis of the latest achievements, the ascertainment of research hotspots, and the discussion of the prospects in the realm of miRNAs in DM are all involved in our study in order to reveal the changes and developments in this realm in the past two decades. Temporarily, both the molecular mechanism of the role of miRNAs in DM and the challenges of clinical trials on miRNAs treating DM and complications of DM are the core research topics in this field. Meanwhile, miRNAs are of great feasibility to be valid for the diagnosis of DM and its complications, such as diabetic nephropathy (DN), diabetic retinopathy (DR), diabetic cardiomyopathy (DCM), etc, but more clinical trials are required to make further proof of miRNAs' usefulness in this regard. Overall, based on our bibliometric study, we believe that miRNAs have been seen to underscore their potential in DM studies by acting as a biomarker for diagnosing diseases, indicating the progression or prognosis of diabetic diseases, and in the treatment of DM. In addition, the field of miRNAs in DM is continuously receiving attention and will be delved deeper into, and more clinical trials will definitely be entered in the future.

## Data Sharing Statement

All data generated or analyzed during this study are included in this article.

## Ethics Approval and Consent to Participate

As this study used publicly available data and involved no human participants, ethical approval was not required.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests in this work.

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