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ORIGINAL ARTICLE

Global research trends on diabetic islet regeneration (2012–2022): a ten-year bibliometric study

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Abstract

Introduction Diabetes mellitus (DM), a prevalent chronic metabolic disorder, has seen an escalating incidence each year, thereby imposing significant burdens on both public health and socio-economic structures. Although numerous outstanding studies have focused on the regeneration of diabetic islets, a gap exists in the form of comprehensive bibliometric analyses in this area.
Methods We employed bibliometric methods to encapsulate and depict the worldwide research directions in this field. Our study engaged in a detailed screening of 552 scholarly articles on diabetic islet regeneration from 2012 to 2022.
Results Our findings indicate a consistent upward trajectory in both publications and citations. Geographically, China holds the forefront in terms of publication volume, followed closely by the United States, India, and Japan. However, in citation quantity, the United States takes the lead, with China, India, and Italy trailing. Institutional contributions are led by the University of Pennsylvania in publication volume, while Harvard University ranks first in citation frequency. Notably, the Journal of Ethnopharmacology emerged as the most prolific journal and achieved a high citation ranking. The current research focal points encompass cell maturation, regenerative medicine, cellular replacement, and gene expression analysis.
Conclusion This study offers an exhaustive bibliometric perspective on the global research trends concerning diabetic islet regeneration over the last decade. It highlights that areas such as beta-cell proliferation, regeneration, and replacement continue to be pivotal in the research landscape for diabetes management.

Keywords Diabetes mellitus · Pancreas · Islet · Regeneration · Bibliometric analysis · Hotspot

Introduction

Diabetes mellitus (DM), an increasingly prevalent chronic metabolic disorder, continues to exert significant strain on global health systems. This disease primarily manifests in two forms: Type 1 diabetes, which arises from autoimmune responses, and Type 2 diabetes, attributed to a combination of insulin resistance and inadequate insulin secretion [1]. The progressive decline in β-cell function is a pivotal element in the pathogenesis of both type 1 and type 2 diabetes [2]. Lifestyle modifications, specifically diet and exercise, form the cornerstone of diabetes management. Alongside these, the administration of oral hypoglycemic agents and exogenous insulin injections constitute the primary medical interventions for DM. However, these strategies often fall short of achieving optimal blood glucose regulation. Consequently, despite these treatments, patients remain susceptible to chronic complications, including diabetic microangiopathy, renal disease, and ocular pathologies [3]. Pancreatic islet and pancreas transplantation face limitations due to surgical complexity, donor shortages, and immune rejection risks, restricting their widespread clinical use [4]. Consequently, identifying safe and effective diabetes treatment methods is of paramount importance.

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In normal physiology, human β-cell proliferation and apoptosis are intricately balanced to maintain homeostasis. However, in diabetic patients, there is a notable reduction in β-cell numbers. Current diabetes treatments fail to address the fundamental pathophysiological changes in diabetic β-cell function. Consequently, targeting the restoration and preservation of β-cell numbers and functionality emerges as a novel and promising approach in diabetes therapy. Despite a surge in research on diabetic islet regeneration, there is a lack of comprehensive studies on progress and emerging trends over the last decade. Our study uses bibliometric analysis to compile and assess publications on diabetic islet regeneration from 2012 to 2022, sourced from the Web of Science Core Collection (WOSCC) database. Visualizing global research trends aims to illuminate the current landscape and guide future investigative directions in diabetic islet regeneration.

Methods

Data collection strategies

Utilizing defined search criteria, we conducted a systematic query for literature on diabetic islet regeneration within the WOSCC database. The search string was as follows: TS = (pancrea* OR islet) AND TS = (regeneration OR repair) AND TS = (diabetes mellitus OR diabet*) AND Language = (English) AND Publication Date = (2012–01-01 to 2022–12-31). Included in our analysis were documents classified as original articles and reviews that conformed to our search criteria. Exclusion criteria encompassed article types such as letters, case reports, withdrawals, bibliography, book chapters, etc., as well as studies published in non-English languages. Both the first author (Yulin Sun) and the corresponding author (Jiachao Xiong) independently performed the data search, eliminating articles not pertinent to the topic. In instances of discrepancy regarding document selection, decisions were reached by consensus among the other two corresponding authors. The comprehensive records of the eligible articles, encompassing details like title, country, keywords, references, and other relevant information, were then downloaded from the WOSCC database.

Bibliometric analysis

For the bibliometric analysis, we employed Microsoft Excel (version 2022), CiteSpace V (version 6.1.2), and VOSviewer (version 1.6.20). Microsoft Excel was utilized to analyze and visualize the annual trends in publication numbers and citations. CiteSpace V and VOSviewer were applied to dissect and graphically represent data related to sources, institutions, countries, references, and keywords. To ensure accuracy and mitigate the potential biases arising from database updates, all analyses were concluded on October 18, 2023. Additionally, the Journal Citation Report was referenced to procure the most recent impact factors (IF) for the year 2022. This comprehensive approach allowed for a thorough and up-to-date bibliometric evaluation of the field.

Results

Global publishing trends

From the WOSCC database, we retrieved 574 articles. After excluding 14 articles types of letters, case reports, withdrawals, bibliography, or book chapters, and 8 articles with publication languages other than English, we included 552 articles. Of these, 418 were original articles and 134 were review articles (Fig. 1). The annual publication output showed a generally ascending trend, with the highest volume in 2022 (Fig. 2A). The annual citation trends also increased over time, reaching a peak in 2022, indicating growing impact and recognition of publications in diabetic islet regeneration.

Analysis of country contributions

In the realm of diabetic islet regeneration research, contributions were made by a total of 63 countries. When setting the minimum publication threshold at five, 31 countries surpassed this benchmark, and their data were subsequently visualized using VOSviewer. The national cooperation network (Fig. 2B) and density heat maps (Fig. 2C) clearly demonstrate that the United States (123 publications, accounting for 22.28% of the total) and China (137 publications, representing 24.82%) are at the core of the collaboration network, exhibiting a high density of publications and robust relationships with other nations. The top ten most productive countries are detailed in eTable 1 (supporting materials 1). Apart from China and the United States, significant contributions came from India (54 publications, 9.78%), Japan (30 publications, 5.43%), and Egypt (25 publications, 4.53%). In terms of citation numbers, the United States leads significantly with 3,152 citations, followed by China with 2,276 citations and India with 811 citations. The overlay visualization of the national cooperation network (Fig. 2D) reveals interesting temporal trends. Countries depicted in purple, such as the United States, Canada, Japan, and India, began publishing in this field as early as 2016. Those shown in green, including China, Spain, and Nigeria, entered the domain primarily in early 2017. Meanwhile, countries represented in yellow, like Iran, Turkey, and Brazil, increased their publication activities post-2018. This temporal distribution underscores the evolving global landscape of research in diabetic islet regeneration.

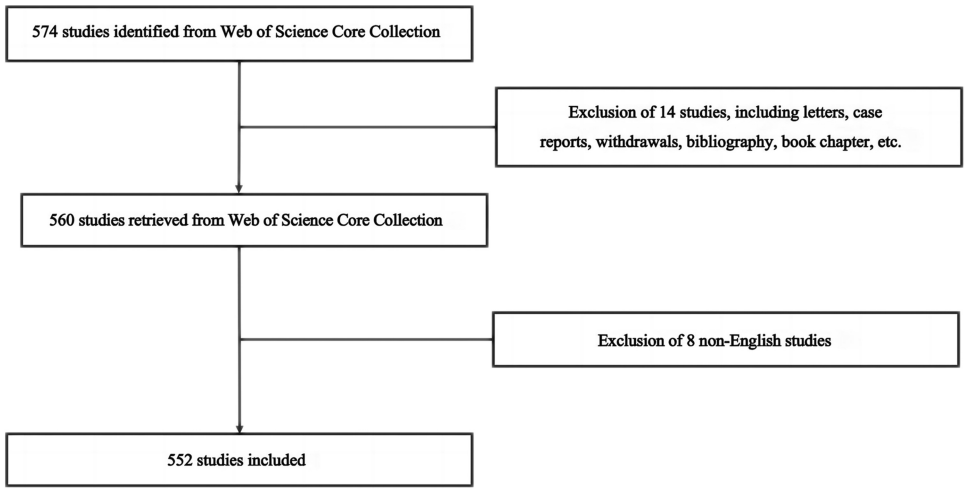

Fig. 1 Flow chart of the data collection method for the investigation of diabetic islet regeneration

Analysis of institution contributions

In the field of diabetic islet regeneration, leading institutions in terms of publication output include the University of Pennsylvania, with 10 publications garnering 490 citations, and Harvard University, contributing 9 publications with 697 citations. Following these are the University of California Los Angeles (UCLA) with 8 publications and 271 citations, and Nanjing University with 7 publications and 150 citations. The top 20 institutions in this field are enumerated in eTable 2 (supporting materials 1). The overlay visualization of the institutional cooperation network

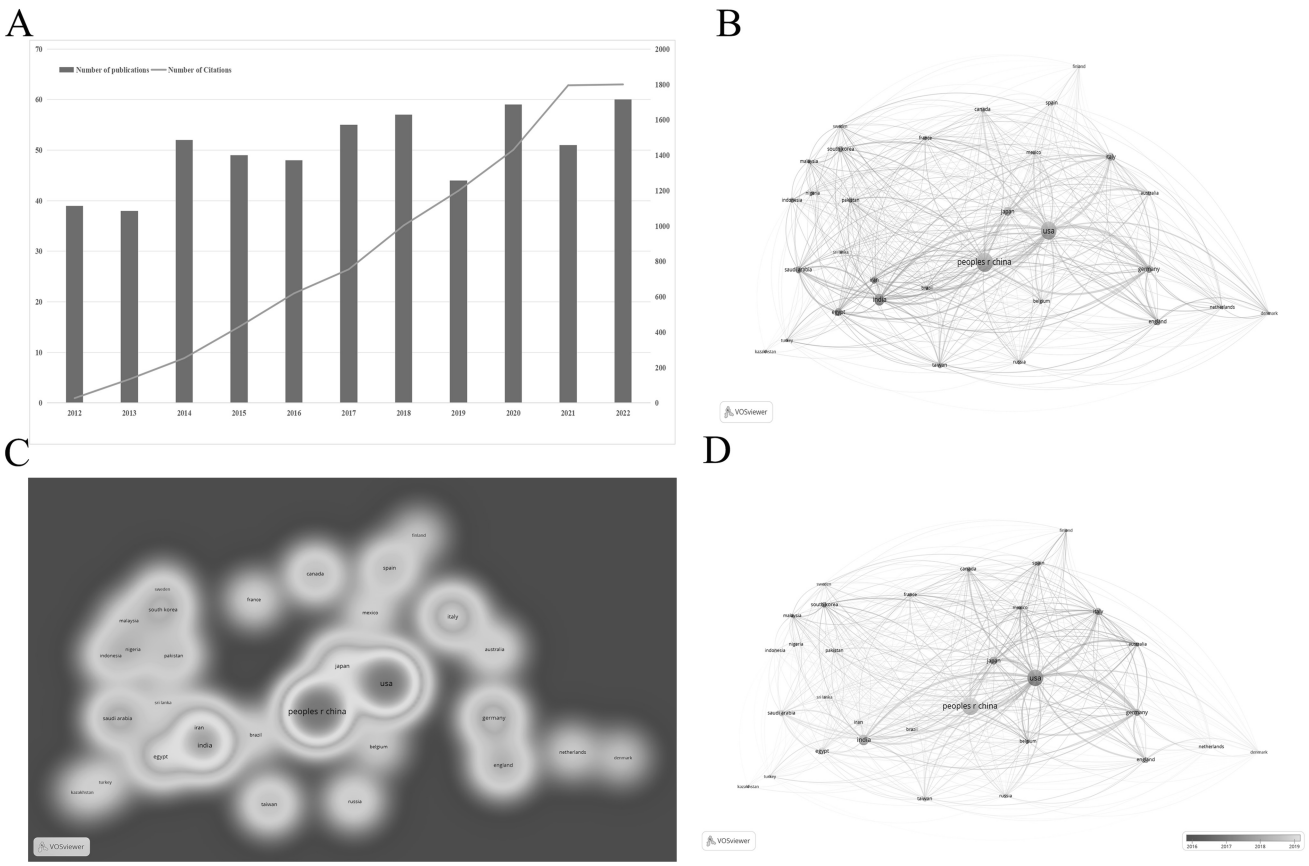

Fig. 2 Global trends in the publication of diabetic islet regeneration. **A** Global trends in the publication and citation of diabetic islet regeneration. **B** Network map of country contributions. **C** Density map of national contributions. **D** Chronological order of national contributions

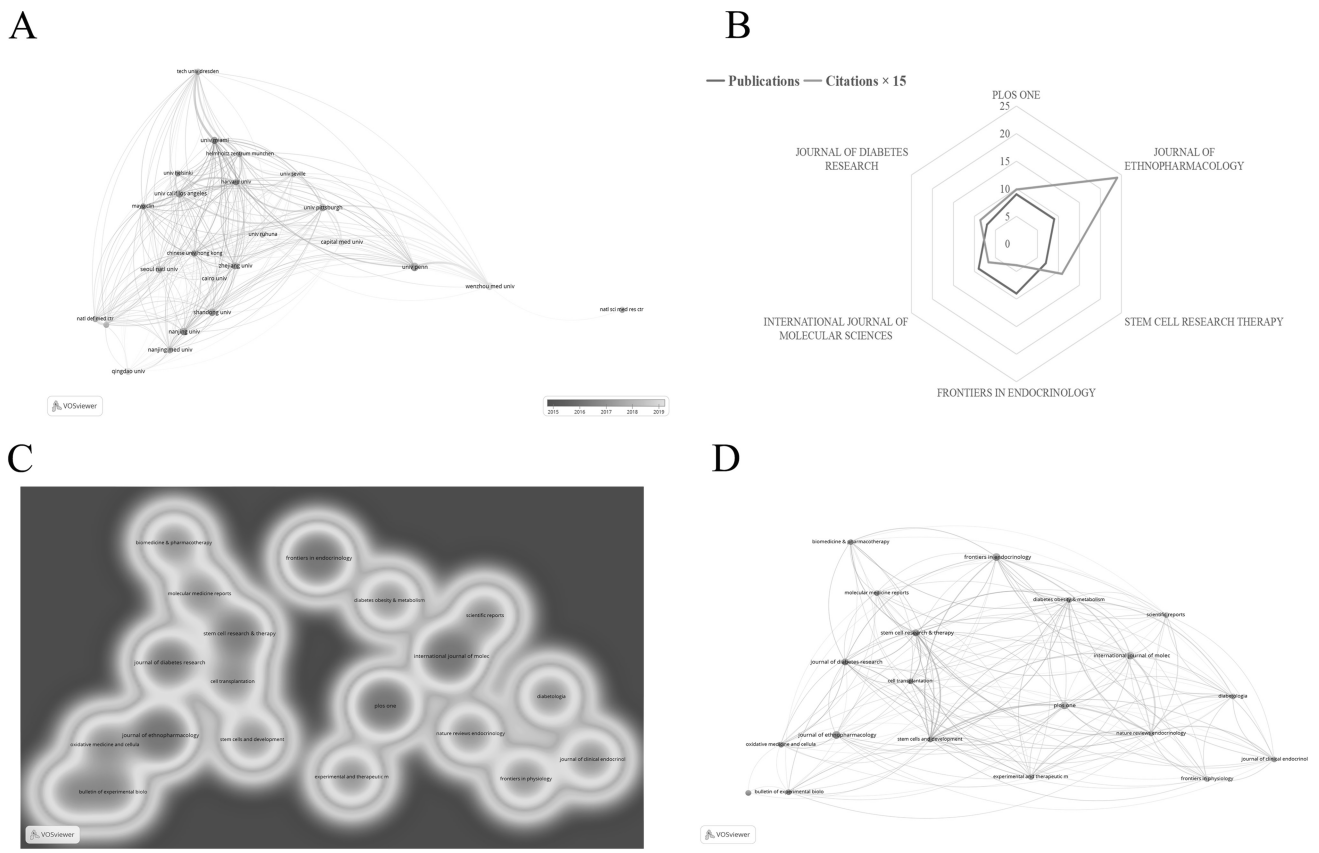

Fig. 3 Global trends in different institutions and journals of diabetic islet regeneration. **A** Network map of contributions from institutions. **B** Radar map displayed the top 7 most productive journals with their publications and citations. **C** Density map of the contributions of the journals. **D** Network map of journal contributions

(Fig. 3A) reveals temporal publication trends among these institutions. Notably, institutions depicted in purple, such as the University of Miami, Mayo Clinic, and Harvard University, primarily commenced their publication contributions after 2015. Those shown in green, including Shandong University, Nanjing University, the University of Seville, and the University of California Los Angeles, were most active between 2016 and 2018. Lastly, institutions represented in yellow, such as Cairo University, Qingdao University, and Capital Medical University, have predominantly increased their publication output post-2018. This temporal analysis provides insights into the evolving collaboration and research dynamics among key institutions in the study of diabetic islet regeneration.

Analysis of journal contributions

In the research domain of diabetic islet regeneration, a total of 327 journals have contributed publications. Applying a minimum criterion of five publications per source, 20 journals surpassed this threshold and their contributions were visualized using Excel and VOSviewer. A radar chart (Fig. 3B) depicts the publication and citation numbers for the top six journals, highlighting their significant roles in the field. The journals that have contributed the most include PLOS One (IF = 3.70, with 9 publications and 148 citations), the Journal of Ethnopharmacology (IF = 5.40, 9 publications, 360 citations), Frontiers in Endocrinology (IF = 5.20, 9 publications, 58 citations), and the International Journal of Molecular Sciences (IF = 5.60, 9 publications, 100 citations). Following these are Stem Cell Research & Therapy (IF = 8.09, 7 publications, 163 citations) and the Journal of Diabetes Research (IF = 4.30, 7 publications, 129 citations). The density heatmaps (Fig. 3C) reveal that PLOS One and the Journal of Ethnopharmacology exhibit a strong publication density. The International Journal of Molecular Sciences demonstrates close relationships with other journals in this field (Fig. 3D). Additionally, eTable 3 (supporting materials 1) lists the top 10 publications with the most citations in diabetic islet regeneration research. This analysis underscores the pivotal role of these journals in advancing and disseminating knowledge in the field.

Analysis of reference contributions

CiteSpace V was utilized to conduct a co-citation analysis of references, the results of which were depicted in a simplified network (Fig. 4A). A seminal article by Pagliuca et al. [5], published in Cell in 2014, emerged as a central node within this network, followed by a significant contribution by Thorel et al. [4] in Nature in 2010. The top 25 references exhibiting the most substantial bursts in citation were identified using a burst algorithm. This method allowed for an analysis of citation trend dynamics, as illustrated in Fig. 4B. Notably, the publication by Ben-Othman et al. [6] in Cell in 2017, which reported the discovery of γ-aminobutyric acid (GABA) as an inducer of α-to-β-like cell conversion in vivo, recorded the highest burst strength of 7.84. This groundbreaking revelation of GABA-induced α cell-mediated β-like cell neogenesis offers novel prospects for diabetes therapy. Further, a title cluster analysis was performed on these references, and the findings were organized chronologically (Fig. 4C). The references were categorized into 11 themes, including diabetic rat, pancreatic stem cell, islet transplantation, cell maturation, regenerative medicine, cell replication, stress-induced adaptive islet cell identity change, myristica fragrans, herbal medicine, pancreatic islet, and pancreatic islet transplantation. Recent trends in the field have particularly focused on topics such as diabetic rat models, cell maturation, regenerative medicine, and myristica fragrans. This analysis provides a comprehensive overview of the evolving research landscape in diabetic islet regeneration.

Analysis of keywords contributions

In our bibliometric analysis of diabetic islet regeneration, a total of 2,888 keywords were identified across publications. By setting a minimum occurrence threshold of 20 for each keyword, 49 keywords surpassed this criterion and were subsequently visualized using VOSviewer (Fig. 5A). These keywords clustered into three distinct groups, with 'regeneration,' 'diabetes mellitus,' 'differentiation,' and 'oxidative stress' emerging as core thematic elements. A further analysis utilizing a burst algorithm was conducted to identify the top 15 keywords with the strongest citation bursts. This approach provided insights into the trends of keyword occurrences, as depicted in Fig. 5B. Notably, 'transdifferentiation,' 'antioxidant activity,' 'obesity,' and 'inflammation' were among the keywords demonstrating significant recent

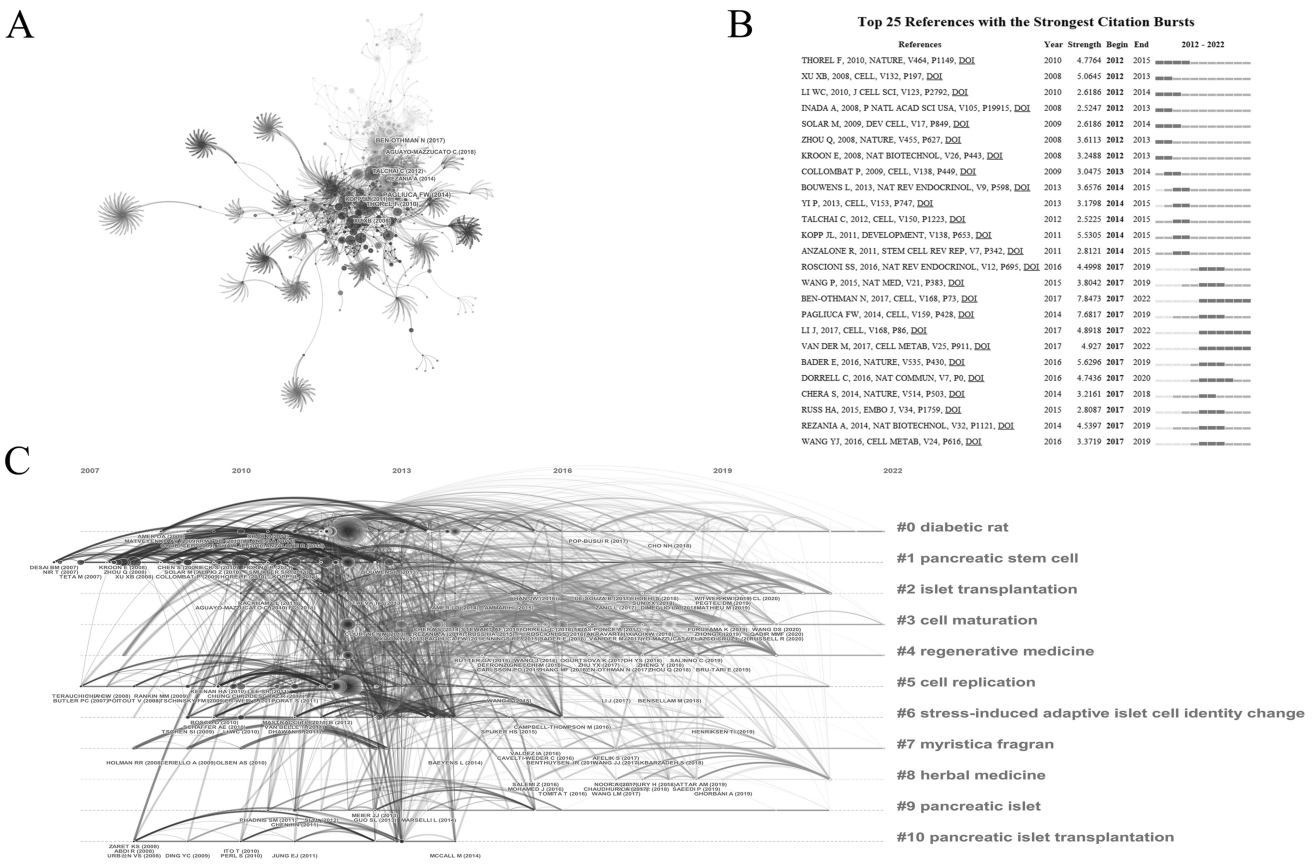

Fig. 4 Global trends in reference to diabetic islet regeneration. **A** A simplified co-citation network of diabetic islet regeneration references. **B** The top 25 references with the strongest citation bursts. **C** Timeline visualization of title cluster analysis result of references

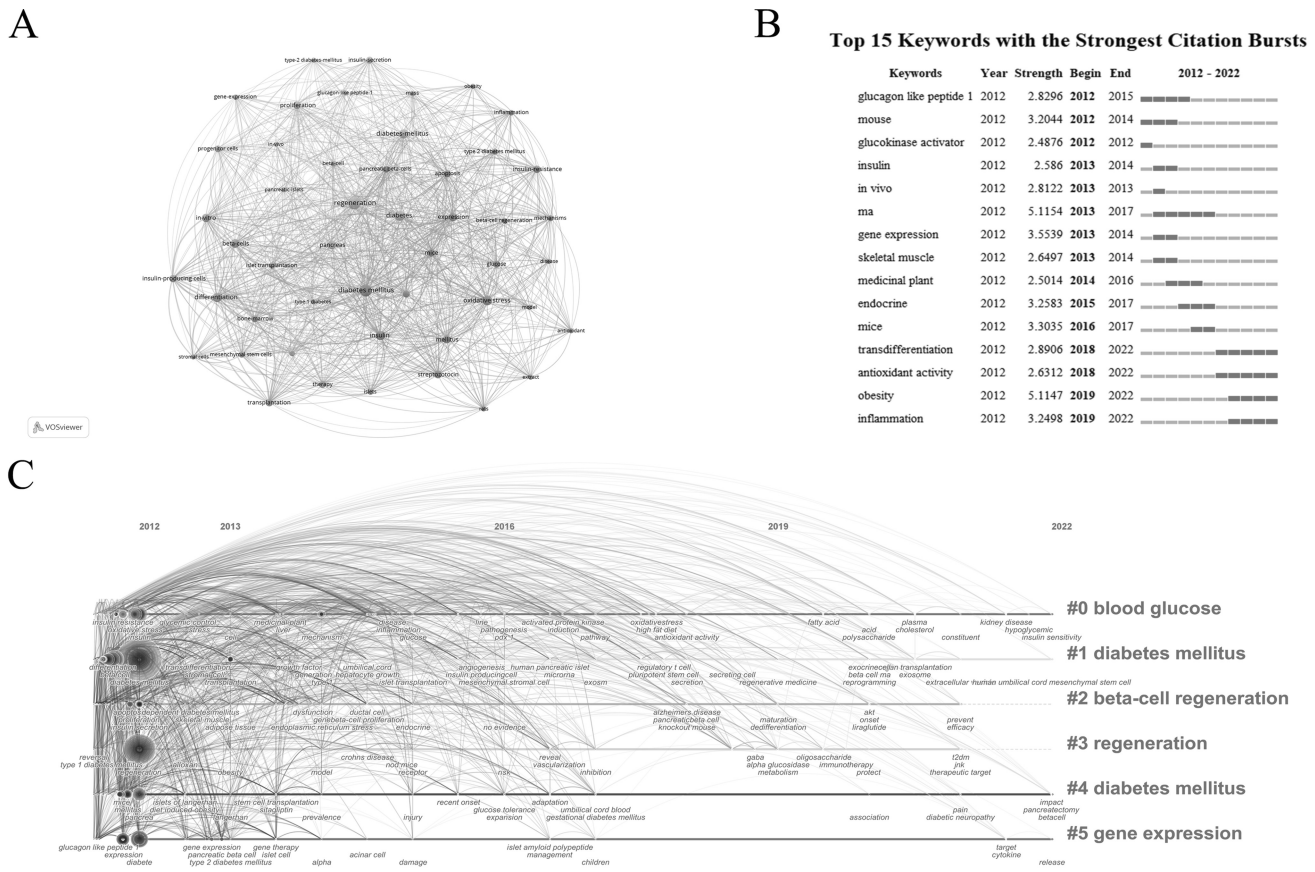

Fig. 5 Global trends in keywords for diabetic islet regeneration. **A** Network map of contributions of keywords. **B** The 15 keywords with the strongest citation bursts. **C** Timeline visualization of keyword cluster analysis result

increases in occurrences. The results of the keyword cluster analysis, arranged on a timeline (Fig. 5C), revealed that the keywords bifurcated into six categories. These encompassed 'blood glucose,' 'diabetes mellitus,' 'beta-cell regeneration,' 'regeneration,' 'diabetes mellitus,' and 'gene expression.' Of these, 'blood glucose,' 'diabetes mellitus,' and 'gene expression' stood out as the most current and active research topics within the field. This keyword analysis underscores the evolving focus areas and may guide future research directions in diabetic islet regeneration.

Discussion

Diabetes has become the third most common non-communicable disease after cancer and cardiovascular disease. This trend underscores the escalating health challenge posed by DM [7–9]. Current clinical treatments for diabetes encompass oral hypoglycemic agents, injectable exogenous insulin, and islet transplantation [10–12]. However, these treatment modalities are associated with challenges such as unstable glycemic control, surgical risks in the case of islet transplantation, and the potential for graft rejection. These factors can complicate the management and effectiveness of diabetes treatment [3, 13]. Type 1 diabetes is typically characterized as a disorder of glucose metabolism caused by the destruction of pancreatic β-cells due to an autoimmune system attack. Dubois et al. [14] found that β-cell count in pancreatic tissue of type 2 diabetes patients was reduced by approximately 60% compared to non-diabetic individuals. However, comprehensive bibliometric analysis in diabetic islet regeneration research is lacking. Our study reviewed 552 publications from 2012 to 2022, employing bibliometric analysis to identify global research trends and provide insights into the current and future directions of this field.

The study observed an increasing trend in diabetic islet regeneration publications and citations from 2012 to 2022 (Fig. 2A). This analysis revealed a steadily increasing trend in publications, with 2022 having the highest number (60, 10.87%) followed by 2020 (59, 10.69%) and 2018 (57, 10.33%). The citation trends also showed rapid growth, peaking in 2022. To understand the global research landscape, a bibliographic coupling analysis of countries was conducted. The US led in both publication quantity and

citations, followed by China, India, and Japan. However, the average citation rate was used to assess the quality of publications from each country (eTable 1). Italy had the highest average citation rate (29.75), followed by the US (25.63) and Germany (25.33). China had the second-highest number of publications but its average citation rate was 16.61, indicating a need to improve the quality of its research to enhance its international impact in diabetic islet regeneration. A bibliographic coupling analysis examined the impact of institutions and journals in the field of diabetic islet regeneration. The University of Pennsylvania and Harvard University were prominent in publications and citations, with Harvard having the highest average citation rate (77.44). The Russian Academy of Sciences, despite contributing 6 publications, had a low average citation rate of 4.33. Key journals like Frontiers in Endocrinology and the Journal of Ethnopharmacology were influential. The top six most productive journals had an Impact Factor (IF) greater than 5, highlighting the current importance of this research topic. The Journal of Ethnopharmacology had the highest average citation rate (40.00), followed by Stem Cell Research & Therapy (23.57), suggesting significant academic influence in this field. For instance, a noteworthy study by Jiao et al. [15] demonstrated that Morus alba fruit polysaccharides, specifically MFP50 and MFP90, exhibited substantial antihyperglycemic and antihyperlipidemic effects. These polysaccharides notably alleviated symptoms in a Type 2 Diabetes Mellitus (T2DM) rat model, indicating their potential as effective treatments for T2DM. Such findings, published in high-impact journals, contribute significantly to the advancement of diabetes treatment research. Moreover, we have observed that the frequency of citations for articles generally correlates positively with the impact factor scores of the journals in which they are published. However, this does not imply that this holds true for all articles. Indeed, there are numerous instances of highly cited papers published in journals with relatively low impact factors, suggesting that the quality of the article itself is a more significant determinant of its citation frequency.

Co-citation analysis of references in our study shows that articles by Thorel and Pagliuca are central to the network, indicating their significant influence and crucial role in diabetic islet regeneration research. These works are frequently cited together by other publications in the field. The research conducted by Thorel et al. [4] significantly contributed to our understanding of the plasticity of pancreatic cells, particularly highlighting the spontaneous transformation among adult endocrine cells. This discovery has provided valuable insights for the treatment of diabetic β-cells. Our analysis, encompassing both title clustering of references and keywords clustering, indicates that the proliferation, regeneration, and replacement of β-cells in diabetic patients continue to be central research themes. Advancements in understanding β-cell development and cell cycle regulation, coupled with high-throughput screening technologies, have facilitated the discovery of new therapeutic targets and small molecules [9]. Despite efforts, challenges in achieving glycemic control in type 1 diabetes mellitus (T1DM) patients through immune attack prevention have necessitated a shift in treatment paradigms [16]. An ideal therapy for T1DM would need to restore immune self-tolerance while replenishing β-cell mass, akin to wound healing processes. In this context, studies demonstrating the potential of bone marrow mesenchymal stem cells to differentiate into insulin-secreting cells under specific inducers or culture systems are particularly noteworthy, as they could provide a sustainable source of donor cells for damaged pancreatic tissue in diabetic patients [17–20]. Additionally, we have compiled a comprehensive overview of clinical research in the field of islet regeneration, which is presented in eTable 4 (supporting materials 1). This compilation serves to better illustrate the current research trends and hotspots within this domain. Stewart et al. [21] focused on therapeutic strategies to increase human β-cell numbers, offering a comprehensive review of key signaling pathways like Janus kinase/signal transducers and activators of transcription, Ras/Raf/extracellular signal-related kinase, cadherins and integrins, G-protein-coupled receptors, and transforming growth factor β, and their relevance to diabetic β-cell regeneration. This work lays a foundational basis for future research in this area. However, challenges persist in maintaining the viability, status, and function of differentiated islet cells, both in vitro and in vivo, which are critical for successful therapeutic applications [22–24]. Additionally, leveraging cutting-edge high-resolution sequencing technologies like single-cell sequencing and spatial transcriptome sequencing to study diabetes pathogenesis is a focal point of current and future research efforts [25]. Furthermore, the application of nanotechnology in diabetic regenerative medicine is ushering in new developments and progress, offering promising avenues for the clinical treatment of diabetes mellitus and its complications.

Conclusion

In summary, this study offers a thorough bibliometric analysis of the global research trends in diabetic islet regeneration over the past decade. We have observed a notable increase in high-quality publications in this field, emphasizing the growing academic and clinical interest. Key areas such as beta-cell proliferation, regeneration, and replacement continue to dominate as focal points for future research in diabetes treatment. This comprehensive analysis not only reflects the current state of the field but also highlights the critical avenues for ongoing and future investigations in diabetic islet regeneration.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13410-024-01341-5.

Author contributions Yulin Sun and Jiachao Xiong had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis; Concept and design: Jiachao Xiong and Hua Jiang; Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Yulin Sun, Lingling Jia and Ying Wang; Tingting Xi and Rong Guo revised manuscript; All authors approved the final version of the manuscript.

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Data Availability The authors confirm that the data supporting the findings of this study are available within the article and supplementary materials.

Declarations

Ethical approval The authors declare human ethics approval was not needed for this study.

Conflict of interest The authors declare no conflict of interests.

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