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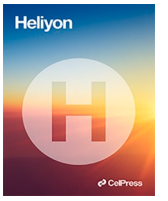

Research article

Influence of glutamine metabolism on diabetes Development:A scientometric review

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ABSTRACT

Objective: "Metabolism affects function" is the consensus of researchers at present. It has potential clinical application value to study the effects of regulating glutamine (Gln) metabolism on diabetes physiology or pathology. Our research aimed to summarize the latest research progress, frontier hot topics and future development trends in this field from the perspective of scientometrics.
Methods: Relevant literatures and reviews were obtained from the Web of Science (WoS) between January 1, 2001 and May 31, 2022. An online analysis platform of bibliometrics, CiteSpace, and VOS viewer software were used to generate visual knowledge network graphs, including publication countries, institutions and authors partnership analysis, co-occurrence analysis, co-citation analysis, as well as citations and keywords burst detection to acquire research trends and hotspots.
Results: Our results showed that a total of 945 publications in the WoS database met the analysis requirements, with articles being the main type. The overall characteristics showed an increasing trend in the number of publications and citations. The United States was leading the way in this research and was a hub for aggregating collaborations across countries. Vanderbilt University delivered high-quality impact with the most published articles. DeBerardinis, RJ in this field was the most representative author and his main research contents were Gln metabolism and mitochondrial glutaminolysis. Significantly, there was a relative lack of collaboration between institutions and authors. In addition, "type 2 diabetes", "glutamine", "metabolism", "gene expression" and "metabolomics" were the keywords categories with high frequency in co-citation references and co-occurrence cluster keywords. Analysis of popular keywords burst detection showed that "branched chain", "oxidative phosphorylation", "kinase", "insulin sensitivity", "tca cycle", "magnetic resonance spectroscopy" and "flux analysis" were new research directions and emerging methods to explore the link between Gln metabolism and diabetes. Overall, exploring Gln metabolism showed a gradual upward trend in the field of diabetes.
Conclusion: This comprehensive scientometric study identified the general outlook for the field and provided valuable guidance for ongoing research. Strategies to regulate Gln metabolism hold promise as a novel target to treat diabetes, as well as integration and intersection of multidisciplinary provides cooperation strategies and technical guarantees for the development of this field.

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1. Introduction

There is a growing body of evidence indicating the significant role of glutamine (Gln) metabolism in conditions like cancer, diabetes and cardiovascular physiology or pathology [1,2]. Gln stands as the predominant amino acid in blood circulation, maintaining a physiological concentration of 0.6 mM in human plasma [3]. With its dual amine and amide functional groups, this non-essential amino acid plays pivotal roles in nitrogen exchange, immunity metabolism and pH homeostasis between organs [4,5]. Metabolism, crucial for cellular functions, sees Gln as a synthetic substrate for deoxyribonucleic acid (DNA), adenosine triphosphate (ATP), proteins and lipids. Consequently, it drives key processes such as cell proliferation, migration, apoptosis, senescence and extracellular matrix deposition. Furthermore, Gln metabolism is metabolised into the tricarboxylic acid (TCA) cycle, providing an energy source building block for proliferating cancer cells [2]. Additionally, Gln exhibits anti-inflammatory and antioxidant effects [6]. Notably, Gln shows promise in mitigating several risk factors associated with cardiovascular diseases, including hypertension, hyperlipidemia, glucose intolerance, obesity and diabetes [7].

Diabetes, better known as diabetes mellitus (DM), has roots in ancient times and is now recognised as a significant threat in the modern era [8]. Hyperglycemia in circulation and its excretion in the urine has been considered a symptom of diabetes in ancient times [9]. While modern medicine views diabetes as a neurometabolic disorder stemming from improper protein-rich diet intake and utilisation, it categorises it into four categories: Type 1 diabetes, Type 2 diabetes, secondary diabetes and gestational diabetes. Diabetes has gained significance as a major threat to human health in the 21st century [10]. Its global prevalence is estimated to soar to 643 million by 2040 [11]. Recent investigations into alternative medicines for preventing, reducing and controlling diabetes have explored the potential of Gln supplementation. A recent review systematically evaluated the potential effects of Gln supplementation on metabolic changes in diabetes, suggesting that Gln supplementation could ameliorate glycemic control, weight management, oxidative stress and inflammatory responses in patients with diabetics [12]. However, the bidirectional communication pathway between Gln metabolism and the diabetic system remains incompletely understood, fuelling a surge in exploratory research in this area. Emerging studies have demonstrated that Gln metabolism is altered in patients with diabetics, evidenced by decreased levels of α-ketoglutarate (α-KG), glutamate and Gln [13]. Furthermore, recent literature suggests that α-KG may hold therapeutic potential in type 2 DM by regulating hepatic glucose metabolism in animals [14]. Therefore, an in-depth understanding of the targets associated with the regulation of Gln metabolism and the changes in its metabolites can unveil the beneficial effects of Gln in this complex metabolic disease, guiding future research endeavours.

The use of scientometrics to visualise information has enabled a multifaceted quantitative and qualitative analysis [15], surpassing traditional literature reviews [16]. This method not only explores and predicts the developmental trajectory of a specific research field [17] but also maps cooperation and contribution levels among different countries, institutions, journals and authors [18]. This study aims to leverage scientometric methods to explore the latest advancements in linking Gln metabolism and diabetes, outlining emerging

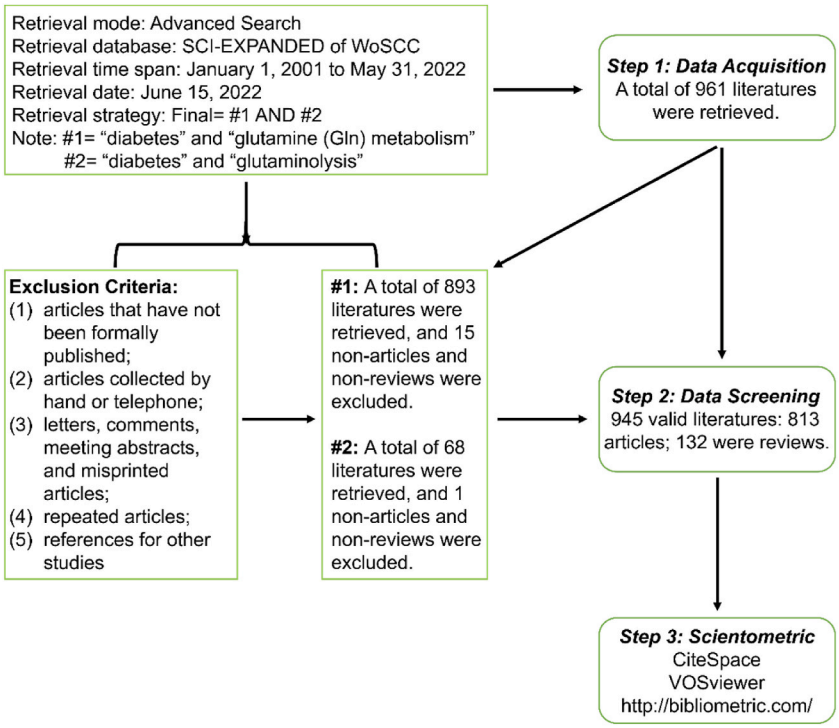

Fig. 1. Flowchart of literature selection and inclusion, exclusion criteria.

topics and applying scientometric methods, outlining emerging topics and predicting future trends. It aims to promote the depth, diversity and international scope of this field of study.

2. Materials and methods

2.1. Data search and collection strategies

The Web of Science (WoS, Clarivate Analytics, Philadelphia, PA, USA) includes the important capabilities of citation indexing and retrieval, and is one of the most authoritative and comprehensive database platforms for obtaining academic information in the world [19], which can be used for the research, analysis and integration of literatures in a certain professional field [15]. In our study, all literatures were searched, downloaded and integrated from the Science Citation Index Expanded (SCIE, 1998-present) of the WoS database. For more efficient and accurate results, search terms included medical subject terms and keywords required for our research. #1 searching for "diabetes" and "glutamine (Gln) metabolism", a total of 893 literatures were retrieved, 15 non-articles and non-reviews were excluded; #2 search for "diabetes" and "glutaminolysis", a total of 68 literatures were retrieved, 1 non-articles and non-reviews was excluded; final dataset is retrieved with #1 AND #2. The complete retrieval process is shown in Fig. 1. We retrieved a total of 961 articles, of which 16 were excluded. Finally, 945 valid documents were obtained as the final dataset and exported in the form of "full records and cited references". Additionally, eligible literature studies were stored in "download_txt" format and exported for further use.

2.2. Criteria for inclusion

The criteria for inclusion were: (1) original peer-reviewed and published articles on diabetes and Gln metabolism AND diabetes and glutaminolysis, including clinical and basic research; (2) reviews on diabetes and Gln metabolism AND diabetes and glutaminolysis; (3) the publication language is only set to English; (4) the search and sort were completed within 1 day, in order to avoid the bias caused by the data update, articles published from January 1, 2001 to May 31, 2022 (searched on June 15, 2022); (5) all literature retrieved from the WoS database.

2.3. Criteria for exclusion

The criteria for exclusion were: (1) articles that have not been formally published; (2) articles collected by hand or telephone; (3) letters, comments, meeting abstracts, and misprinted articles; (4) repeated articles; and (5) references for other studies [16,20], two independent researchers reviewed article titles, abstracts, etc., and deleted articles that were not related to diabetes and Gln metabolism AND diabetes and glutaminolysis.

The flowchart of the specific search strategy, inclusion and exclusion results is shown in Fig. 1.

2.4. Data extraction

Literatures retrieved from WoS were imported into CiteSpace version 5.8. R2 (Chaomei Chen, Drexel University, USA) to remove duplicate literature materials [16]. Data curation was performed by other investigators to ensure the accuracy and reliability of the data ultimately used for analysis. The data we extracted include the number of citations, countries/regions, institutions, authors, subject categories, published journals, frequently cited articles, references, and keywords, etc. [15]. From the information provided in the 2021 Journal Citation Reports (JCR, Clarivate Analytics, Philadelphia, PA, USA), we obtain the impact factor (IF), quartile in category (Q1, Q2, Q3 and Q4) and other indicators of the published journals.

2.5. Data analysis and visualization

This study uses three bibliometric tools for scientometric analysis and visualization. CiteSpace, is one of the most used bibliometric tools to determine the development, distribution, and change in a field of research [21]. In this study, the parameters of CiteSpace are as follows: the time span is 2001.1–2022.5.31, each film year is set to 1, and the selection criterion is the top 25. In the visualised network graph, nodes represent countries, institutions or authors. The size of the nodes and the different colored rings indicate the number and different years of these factors, respectively. The lines between nodes reflect the cooperative or co-citation relationship in factors [22,23].

VOSviewer 1.6.17.0 (Van Eck and Waltman, Leiden University, Netherlands) has the function of literature in-depth mining [24], which can extract important parameters from a large number of scientific publications for mapping co-citation and co-occurrence network graphs visualization [15]. In our study, this software was used to draw a visual network diagram, including institutional analysis, author analysis, journal co-citation analysis, and keyword co-occurrence analysis. The network graph parameters for keyword co-occurrence analysis were as follows: the minimum number of occurrences of keywords was 5, and the resolution was 0.7. In addition, VOS viewer can provide three types of network maps, namely network visualization map, overlay visualization map, and density visualization map [25].

An online analysis platform of bibliometrics (http://bibliometric.com/) was also used for annual publication trend analysis and cooperation strength of various countries analysis.

Moreover, Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA) and GraphPad Prism version 8.0. (GraphPad Software, La Jolla, USA) were used to analyze and create a graph of the distribution of literature types, a trend chart of changes of the annual number of publications, and total number of documents issued in the top ten countries/regions in this field.

3. Results

3.1. Statistics of article publications and assessment of future growth trends

The number of articles published in a scientific field offers insights into its developmental trajectory. In this study, a total of 945 articles were retrieved— 813 original articles (86.03 %) and 132 reviews (13.97 %) (Fig. 2A). Bibliometrics, using an online platform, was used to count the actual number of articles published annually in this field (Fig. 2B). The histogram illustrates a consistent overall upward trend in the total number of articles published, peaking at 85 publications in 2017 (8.99 % of the total). Notably, the absence of articles in the field during the early period (2001–2006) preceded a rapid increase post-2007. This surge mirrors the increase in the exploration of 'metabolism affects diseases' in modern medicine, drawing considerable attention to the role of Gln metabolism in diabetes. Recent studies have gradually revealed the pathogenesis and target of Gln metabolism in diabetes [13,26,27]. Additionally, a summary of the top 9 most frequently cited papers in this field (Table 1) offers a comprehensive reference for future research directions.

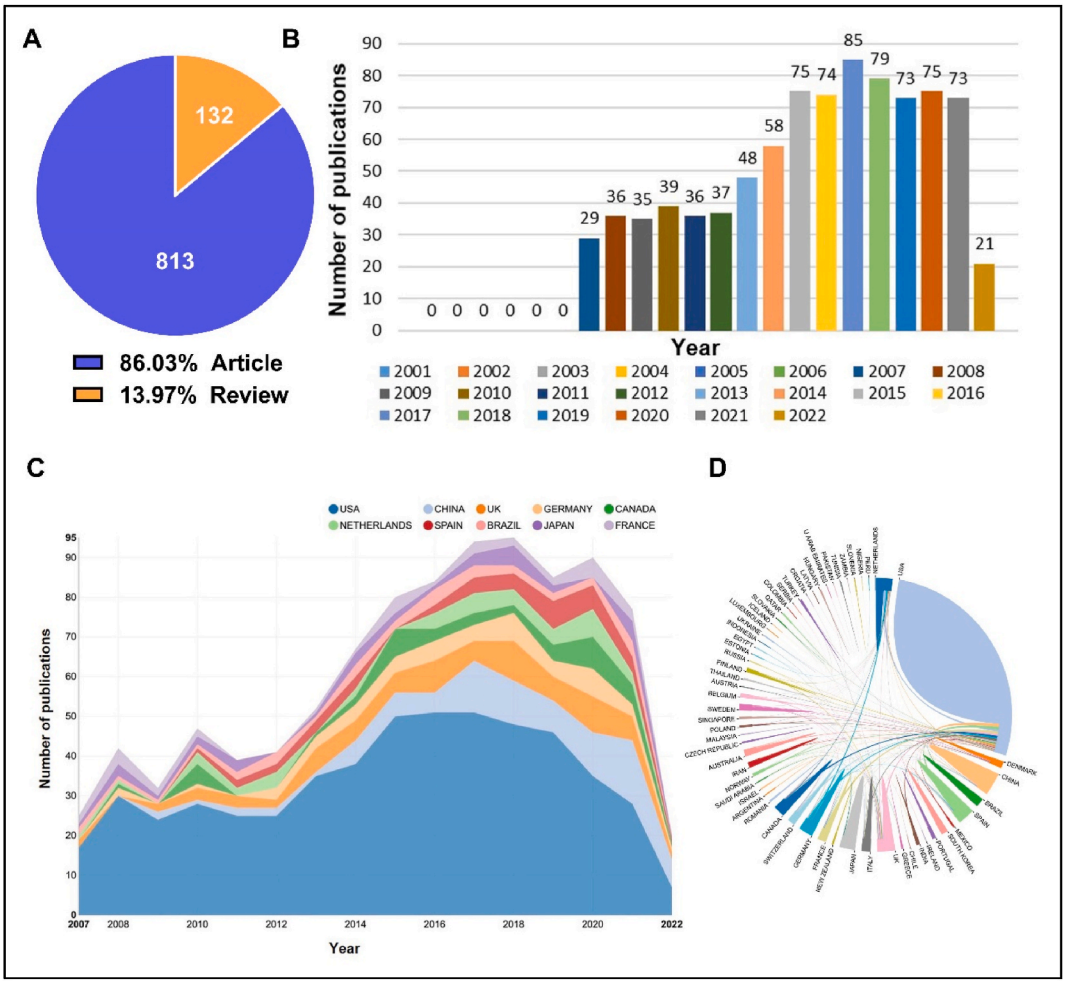

Fig. 2. Types of literature and number of publications per year on diabetes and Gln metabolism AND diabetes and glutaminolysis from 2001 to 2022. **(A)** Distribution map of literature types, *orange* for reviews and *blue* for articles. **(B)** The annual number and growth trend of articles published on the topics of diabetes and Gln metabolism AND diabetes and glutaminolysis from 2001 to the first half of 2022, statistics from the Online Analysis Platform of Literature Metrology. **(C)** The number of articles published in the top 10 countries/regions with the most research achievements in diabetes and Gln metabolism AND diabetes and glutaminolysis from 2001 to 2022, the area graph reflects the number of online articles per year, statistics from the online analysis platform of literature metrology. **(D)** International collaboration analysis among different countries. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

To identify research countries/regions that contribute significantly to this field, we analysed the number of articles published in different countries/regions. The top 10 countries/regions publishing the most reports in the past 20 years are presented in the area chart (Fig. 2C). The United States was revealed as a pioneer in this field. While the United States sustained steady growth in publications, China, the United Kingdom and Germany have joined the forefront since 2013, with China experiencing rapid growth since 2017. Expectations are high for a further surge in the number of Chinese publications. The interconnection and cooperation between different countries are displayed in Fig. 2D. The line thickness between different countries indicates the strength of cooperation between the two countries. Currently, the United States closely collaborates with China, Spain, France, Canada and Germany. Overall, strengthening these international connections remains pivotal for future progress.

Table 1
Top 9 most frequently cited papers in the field of diabetes and Gln metabolism AND diabetes and glutaminolysis.

Rank	Times Cited	Title	Year	Journal			
				Name	JCR (2022)	IF (2022)	Main Conclusions
1	75	Beyond aerobic glycolysis: Transformed cells can engage in glutamine metabolism that exceeds the requirement for protein and nucleotide synthesis [28]	2007	*Proceedings of the National Academy of Sciences of the United States of America*	Q1	11.1	The result demonstrate that Gln metabolism provides a carbon source that facilitates the cell's ability to use glucose-derived carbon and TCA cycle intermediates as biosynthetic precursors.
2	67	Understanding the Warburg Effect: The Metabolic Requirements of Cell Proliferation [29]	2009	*Science*	Q1	56.9	The data propose that the metabolism of cancer cells is adapted to facilitate the uptake and incorporation of nutrients into the biomass needed to produce a new cell.
3	60	c-Myc suppression of miR-23 enhances mitochondrial glutaminase and glutamine metabolism [30]	2009	*Nature*	Q1	64.8	The result provide that a regulatory mechanism involving Myc and miRNAs for elevated expression of glutaminase and Gln metabolism in human cancers, uncover a pathway by which Myc suppression of miR-23, which targets GLS, enhances Gln catabolism through increased mitochondrial glutaminase expression.
4	57	Myc regulates a transcriptional program that stimulates mitochondrial glutaminolysis and leads to glutamine addiction [31]	2008	*Proceedings of the National Academy of Sciences of the United States of America*	Q1	11.1	The data suggest that oncogenic levels of Myc induce a transcriptional program that promotes glutaminolysis and triggers cellular addiction to Gln as a bioenergetic substrate.
5	57	Reductive glutamine metabolism by IDH1 mediates lipogenesis under hypoxia [32]	2011	*Nature*	Q1	64.8	The result identify a critical role for oxygen in regulating carbon use to produce AcCoA and support lipid synthesis in mammalian cells.
6	54	A Branched-Chain Amino Acid-Related Metabolic Signature that Differentiates Obese and Lean Humans and Contributes to Insulin Resistance [33]	2009	*Cell Metabolism*	Q1	29	The finding show that in the context of a poor dietary pattern that includes high fat consumption, BCAA contributes to development of obesity-associated insulin resistance.
7	50	Metabolite Profiles and the Risk of Developing Diabetes [34]	2011	*Nature Medicine*	Q1	82.9	The finding underscore the potential importance of amino acid metabolism early in the pathogenesis of diabetes, and suggest that amino acid profiles could aid in diabetes risk assessment.
8	44	Reductive carboxylation supports growth in tumor cells with defective mitochondria [35]	2011	*Nature*	Q1	64.8	The result demonstrate that during malignant transformation the acquisition of somatic mutations that impair mitochondrial function and stimulate aerobic glycolysis does not diminish the importance of Gln metabolism or of the mitochondria themselves for tumor cell proliferation.
9	44	The Biology of Cancer: Metabolic Reprogramming Fuels Cell Growth and Proliferation [36]	2008	*Cell Metabolism*	Q1	29	This review examines the idea that several core fluxes, including aerobic glycolysis, de novo lipid biosynthesis, and Gln-dependent anaplerosis, form a stereotyped platform supporting proliferation of diverse cell types.

3.2. Analysis of countries/regions and institutions cooperation

Employing CiteSpace, we analysed the collaboration between countries/regions or between institutions, revealing a network of 59 countries/regions (Figs. 2D) and 1302 contributing institutions. Table 2 summarises the top 20 high-yield institutions based on publication volume. Vanderbilt University emerged as the institute with the highest number of articles published in the field of Gln metabolism and diabetes (90, 9.52 %), followed by Yale University (79, 8.36 %), University of Texas Southwestern Medical Center (76, 8.04 %), University of Pennsylvania (72, 7.62 %), Emory University (57, 6.03 %) and University of Michigan (57, 6.03 %). The dominance of the United States in terms of publication volume solidifies its academic influence in this field.

Fig. 3A displays a map of the cooperation network between countries. In terms of publications and centrality, the United States emerges as the most academically influential country in the field. Additionally, an analysis using VOS viewer reaffirmed the United States' dominant position (Supplementary Fig. 1). Moreover, the development and level of scientific research in a country also reflect its comprehensive strength. There exist significant differences in the distribution of the gross domestic product (GDP) to scientific research. According to the latest global GDP (2022) ranking of various countries and the map of the cooperation networks among countries in this field, the United States ($22.94 trillion), which ranks first in GDP, maintained leadership, collaborating extensively across countries. China ($16.86 trillion), which ranks second in GDP, and Germany ($4.23 trillion), which ranks fourth, also engaged significantly in this research field. Encouraging closer communication and reference exchange between low - and middle-income countries with high-income counterparts promises to elevate scientific research. Fig. 3B presents clusters of institutional collaborations in Gln metabolism and diabetes research. The size of the concentric circles denotes the number of published articles (the greater the number of published articles, the larger the concentric circles of their institutions), while lines connecting the two institutions represent collaborative publications (the stronger the line, the greater the collaborative strength).

3.3. Author contribution analysis

The higher the number of articles published by an author, the greater the scholarly activity and contribution to the respective research field. Based on the publication count (Table 3), Nissim, I emerged as the most prolific author with 20 publications, followed by Weiner, ID (18 publications) and DeBerardinis, RJ (17 publications).

Each author brings unique professional characteristics to diverse research topics, and cross-collaboration among them fosters interaction and increased quantitative output in this domain. Additionally, analysing an author and his co-authors provides an understanding of existing partnerships, thereby aiding in further communication and potential collaborative theme development [15]. As shown in Fig. 4, a visual map of the collaboration between authors generated by the VOS viewer showcases several concentrated research groups with distinct clusters of closely collaborating authors. Groups in each collection are connected by one or two core authors with outstanding contributions, like Nissim, I; Weiner, ID; DeBerardinis, RJ and Rothman, DL. Notably, DeBerardinis, RJ and Nissim, I have closely collaborated, revealing insights into how glutamine metabolism facilitates cells to utilise carbon sources from glucose and TCA cycle intermediates for biosynthesis [28]. Collaboration between authors tends to center on fundamental research articles, indicating a need for stronger inter-group connections in this field. Thus, efforts should focus on fostering better exchanges and connections among these ensemble groups. Additionally, CiteSpace was employed to identify mutual collaborations among authors, producing results consistent with those described above (Supplementary Fig. 2).

Table 2
Top 20 institutions with the most publications related to diabetes and Gln metabolism AND diabetes and glutaminolysis research.

Ranking	Location	Institution	Count	Percentage (% of 945)	Average Citations per Item	Sum of Times Cited
1	United States	Vanderbilt Univ	90	9.52	1.77	159
2	United States	Yale Univ	79	8.36	2.94	232
3	United States	Univ Texas SW Med Ctr Dallas	76	8.04	10.25	779
4	United States	Univ Penn	72	7.62	4.18	301
5	United States	Emory Univ	57	6.03	0.91	52
6	United States	Univ Michigan	57	6.03	0.67	38
7	United States	Harvard Med Sch	53	5.61	0.85	45
8	United States	Univ Louisville	43	4.55	3.86	166
9	Netherlands	Leiden Univ	43	4.55	0.21	9
10	United States	Univ Florida	42	4.44	2.86	120
11	United States	Duke Univ	36	3.81	1.25	45
12	Denmark	Univ Copenhagen	34	3.60	1.62	55
13	United States	Childrens Hosp Philadelphia	31	3.28	7.11	220
14	United States	Univ Calif San Diego	31	3.28	2.52	78
15	United States	Johns Hopkins Univ	31	3.28	1.68	52
16	United States	Univ Kentucky	31	3.28	1.13	35
17	United States	Univ Alabama Birmingham	30	3.17	1.21	36
18	United States	Univ Washington	30	3.17	0.53	16
19	United States	Univ Calif Davis	29	3.07	2.14	62
20	United States	MIT	28	2.96	10.96	307

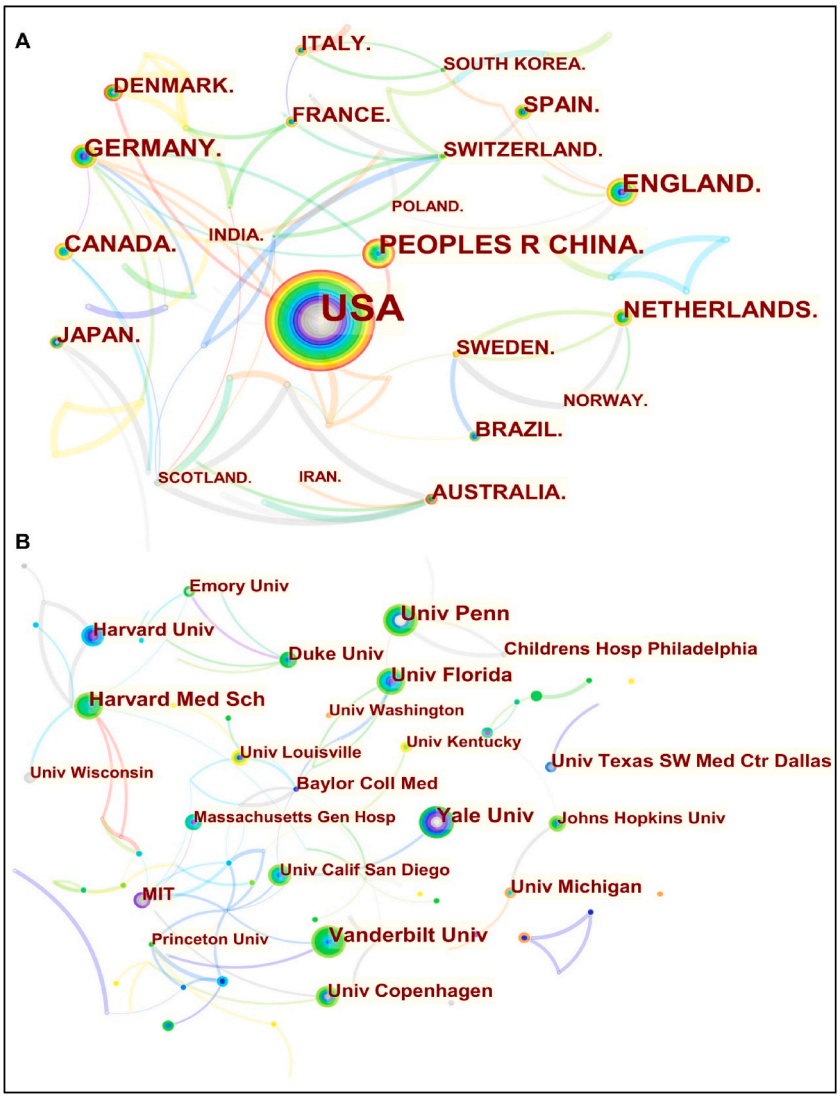

Fig. 3. Visual knowledge maps of mutual cooperation on diabetes and Gln metabolism AND diabetes and glutaminolysis from 2001 to 2022. (A) Analytical network map of mutual cooperation between countries. (B) Analytical network map of mutual cooperation between institutions. The different circles in the diagram represent a country or institution. The larger the circle area, the more articles are published; the lines between the circles indicate mutual cooperation; the circle with high centrality is at an important core position.

Table 3
Top 10 authors with the most publications related to diabetes and Gln metabolism AND diabetes and glutaminolysis research.

Ranking	Author	Total publications	Citations
1	Nissim, I	20	151
2	Weiner, ID	18	104
3	DeBerardinis, RJ	17	333
4	Verlander, JW	16	89
5	Rothman, DL	16	46
6	Lee, HW	14	71
7	Behar, KL	14	45
8	Stephanopoulos, G	12	134
9	Metallo, CM	12	108
10	Mason, GF	11	38

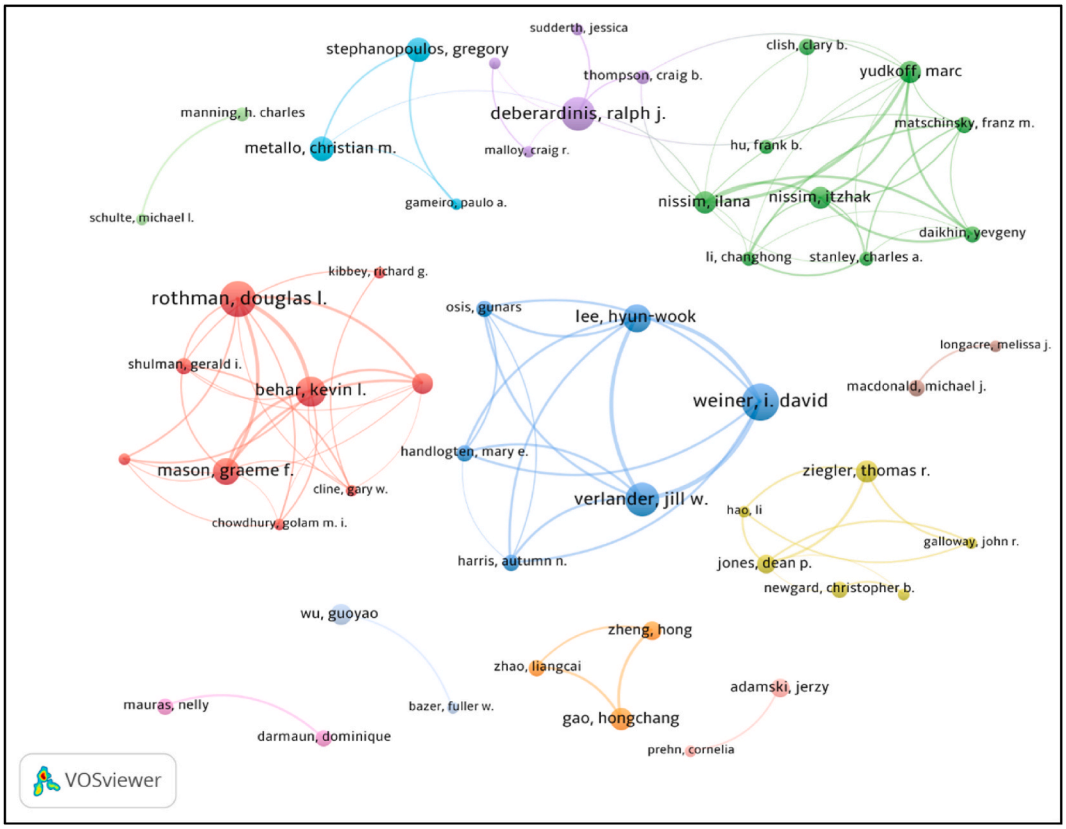

Fig. 4. Collaboration analysis network map of authors on diabetes and Gln metabolism AND diabetes and glutaminolysis from 2001 to 2022.

3.4. Analysis of the higher-impact journals

Journal publications significantly influence scientific communication, reference and citation practices. Analysing journal sources aid in identifying appropriate and suitable platforms for publication and fostering effective scholarly communication [15,19]. Among the 379 journals publishing articles on Gln metabolism and diabetes research, many of them were specialised academic journals. As

Table 4
Top 20 journals with the most total citations in the field of diabetes and Gln metabolism AND diabetes and glutaminolysis research.

Ranking	Journal Name	Citations	Count	Percentage (% of 945)	IF (2021)	JCR (2021)
1	*Proceedings of the National Academy of Sciences of the United States of America*	174	14	1.48	11.205	Q1
2	*Nature*	126	6	0.63	49.962	Q1
3	*Cell Metabolism*	123	20	2.12	27.287	Q1
4	*American Journal of Physiology-Renal Physiology*	72	15	1.59	3.377	Q2
5	*Journal of Biological Chemistry*	57	31	3.28	5.157	Q1
6	*Oncogene*	43	3	0.32	9.867	Q1
7	*Journal of Cerebral Blood Flow and Metabolism*	34	10	1.06	6.200	Q1
8	*Amino Acids*	29	6	0.63	3.520	Q2
9	*Cancer Research*	29	9	0.95	12.701	Q1
10	*Plos One*	26	29	3.07	3.240	Q1
11	*Nutrition*	26	9	0.95	4.008	Q2
12	*Journal of Clinical Investigation*	26	4	0.42	14.808	Q1
13	*Diabetologia*	24	8	0.85	10.122	Q1
14	*Diabetes*	22	14	1.48	9.461	Q1
15	*Current Opinion in Genetics & Development*	21	2	0.21	5.578	Q2
16	*Clinical Journal of the American Society of Nephrology*	19	2	0.21	8.237	Q1
17	*Journal of Neurochemistry*	18	4	0.42	5.372	Q2
18	*Journal of Clinical Endocrinology & Metabolism*	17	10	1.06	5.958	Q1
19	*Nutrition & Metabolism*	16	3	0.32	4.169	Q3
20	*Molecular Systems Biology*	13	1	0.11	11.429	Q1

shown in Supplementary Table 1, the three most influential journals publishing the relevant articles were the *Journal of Biological Chemistry* (31), *Plos One* (29) and *Cell Metabolism* (20). However, the impact of journals does not depend solely on the number of articles published; it is also gauged by the frequency of co-citations within the research field [25]. Table 4 lists the top 20 most cited journals. Among them, the top five journals with the most citations are *Proceedings of the National Academy of Sciences of the United*

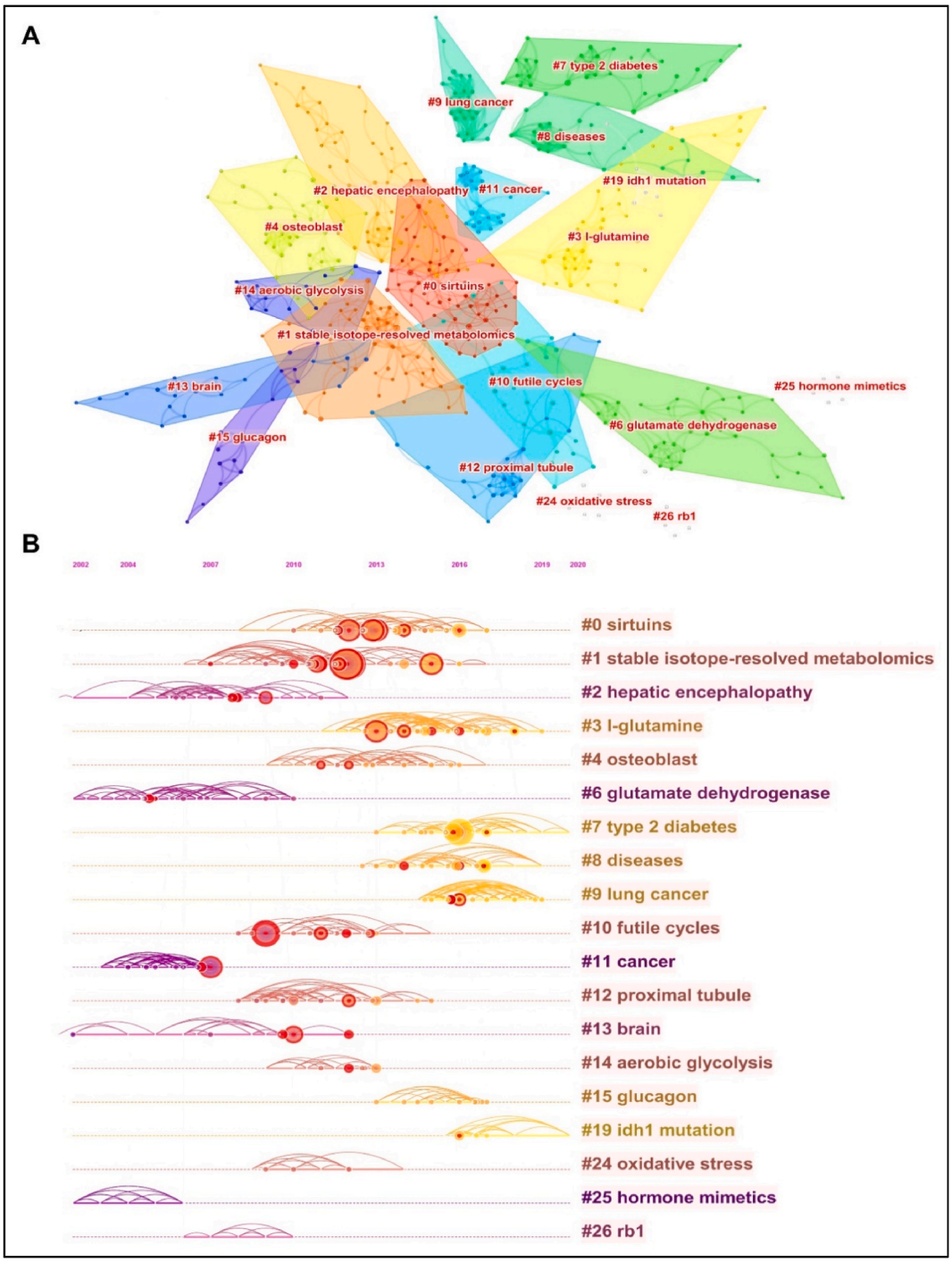

Fig. 5. Reference co-citation visualization network knowledge map for diabetes and Gln metabolism AND diabetes and glutaminolysis research from 2001 to 2022. (A) Reference co-referenced aggregate taxonomy visualization map, labeled with all 19 aggregate taxonomies. Different colors represent different clusters. (B) Timeline visualization plot of reference co-citation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

States of America (174 citations), *Nature* (126 citations), *Cell Metabolism* (123 citations), *American Journal of Physiology-Renal Physiology* (72 citations) and *Journal of Biological Chemistry* (57 citations). These journals have garnered substantial attention and citations due to high-profile research contributions in this field.

The impact factor (IF), introduced by Garfield in 2006, measures the average citation frequency of articles published by the journal in a given year, offering insights into the journal's relative importance within its research field [37]. Among the top 20 most cited academic journals, *Nature* (IF = 49.962) has the highest IF, followed by *Cell Metabolism* (IF = 27.287), *Journal of Clinical Investigation* (IF = 14.808), *Cancer Research* (IF = 12.701) and *Molecular Systems Biology* (IF = 11.429). JCR is an effective tool for systematic and objective evaluation of authoritative journals worldwide [38]. JCR divided journals in the same category into four equal quartiles– Q1 representing the top 25 %, Q2 representing the top 25 50 %, and so forth [39]. Notably, 70 % of these journals belong to Q1, indicating their potential for publishing high-quality research and enhancing the field's influence and development prospects in the future (Table 4). Furthermore, a co-citation analysis conducted using the VOS viewer unveils connections among different journals published in this research area from 2001 to 2022 (Supplementary Fig. 3), identifying pivotal professional journals for researchers in this field.

Table 5
The top 10 co-cited references in the field of diabetes and Gln metabolism AND diabetes and glutaminolysis.

Rank	Title	Type of Document	Year	Journal			
				Name	JCR (2022)	IF (2022)	Main Conclusions
1	Reductive glutamine metabolism by IDH1 mediates lipogenesis under hypoxia [32]	Article	2011	*Nature*	Q1	64.8	The result identify a critical role for oxygen in regulating carbon use to produce AcCoA and support lipid synthesis in mammalian cells.
2	Beyond aerobic glycolysis: Transformed cells can engage in glutamine metabolism that exceeds the requirement for protein and nucleotide synthesis [28]	Article	2007	*Proceedings of the National Academy of Sciences of the United States of America*	Q1	11.1	The result demonstrate that Gln metabolism provides a carbon source that facilitates the cell's ability to use glucose-derived carbon and TCA cycle intermediates as biosynthetic precursors.
3	Understanding the Warburg Effect: The Metabolic Requirements of Cell Proliferation [46]	Review	2009	*Science*	Q1	56.9	The data propose that the metabolism of cancer cells is adapted to facilitate the uptake and incorporation of nutrients into the biomass needed to produce a new cell.
4	Reductive carboxylation supports growth in tumor cells with defective mitochondria [32]	Article	2011	*Nature*	Q1	64.8	The result demonstrate that during malignant transformation the acquisition of somatic mutations that impair mitochondrial function and stimulate aerobic glycolysis does not diminish the importance of Gln metabolism or of the mitochondria themselves for tumor cell proliferation
5	From Krebs to clinic: glutamine metabolism to cancer therapy [47]	Review	2016	*Nature*	Q1	64.8	The result demonstrate that targeting Gln metabolism shows promise as an anticancer therapy.
6	Hypoxia promotes isocitrate dehydrogenase-dependent carboxylation of α-ketoglutarate to citrate to support cell growth and viability [42]	Article	2011	*Proceedings of the National Academy of Sciences of the United States of America*	Q1	11.1	The data support a role for Gln carboxylation in maintaining citrate synthesis and cell growth under hypoxic conditions.
7	Glutamine and cancer: cell biology, physiology, and clinical opportunities [43]	Review	2013	*The Journal of Clinical Investigation*	Q2	15.9	Review the metabolic functions of Gln as a super nutrient and the surprising roles of Gln in supporting the biological hallmarks of malignancy.
8	Glutamine supports pancreatic cancer growth through a KRAS-regulated metabolic pathway [44]	Article	2013	*Nature*	Q1	64.8	The result demonstrate that reprogramming of Gln metabolism is mediated by oncogenic KRAS,
9	Antitumor Activity of the Glutaminase Inhibitor CB-839 in Triple-Negative Breast Cancer [45]	Article	2014	*Molecular Cancer Therapeutics*	Q2	5.7	The data provide a strong rationale for the clinical investigation of CB-839 as a targeted therapeutic in patients with TNBC and other Gln-dependent tumors.
10	Pyruvate carboxylase is critical for non–small-cell lung cancer proliferation [48]	Article	2015	*The Journal of Clinical Investigation*	Q2	15.9	The finding indicate that PC-mediated anaplerosis in early-stage non-small-cell lung cancer is required for tumor survival and proliferation.

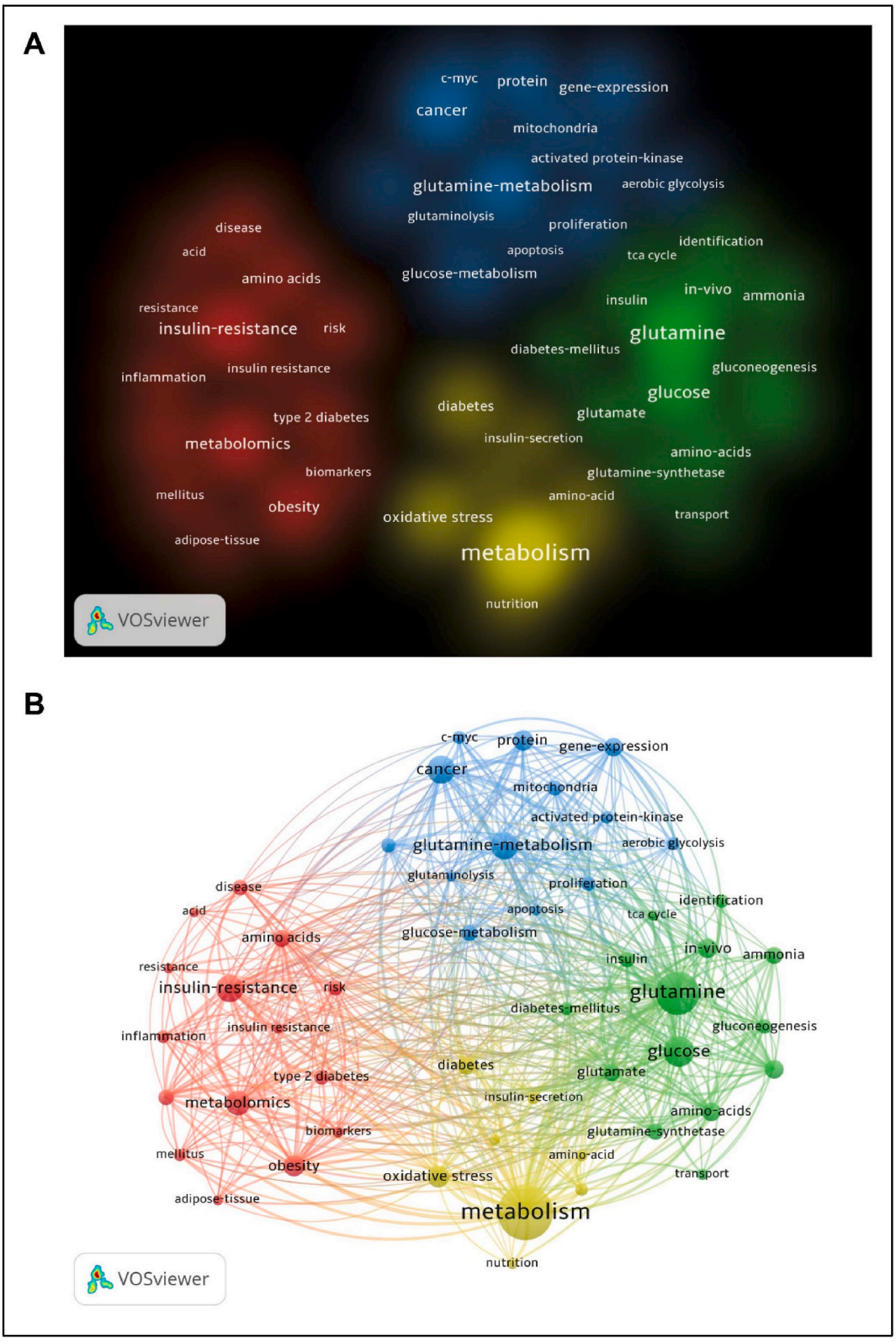

Fig. 6. Visual map of keyword co-occurrence analysis from 2001 to 2022, analysed by VOS viewer software. **(A)** Density visualization map, the depth of color is positively correlated with the frequency of keyword occurrence. **(B)** Network visualization map, keywords can be aggregated into four categories. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3.5. Analysis of co-citation references

Reference co-citation analysis assesses documents cited concurrently, revealing their interconnectedness and indicating authoritative research and significant author contributions [40]. Using CiteSpace software with a time slice of one year and a period from 2001 to 2022, a co-citation network map of the cited references, presented in the form of abbreviated references, was generated, demonstrating interconnections among the co-cited references (Supplementary Fig. 4). By extracting and analysing these references, a visualised network map of cited references emerged (Fig. 5A). Employing the software to perform cluster function analysis, the entire network was aggregated into several different clusters, and the largest 19 clusters in this field were extracted using the log-likelihood ratio algorithm (LLR).,Fig. 5A shows the clusters with different analogies, namely sirtuins (cluster #0), stable isotope-resolved metabolomics (cluster #1), hepatic encephalopathy (cluster #2), L-glutamine (cluster #3), osteoblast (cluster #4), glutamate dehydrogenase (cluster #6), type 2 diabetes (cluster #7), diseases (cluster #8), lung cancer (cluster #9), futile cycles (cluster #10) and so on. Additionally, two important parameters used for evaluating the aggregated community structure were the modularity value (Q-value) and the mean contour value (S-value), where $Q > 0.3$ and $S > 0.5$ indicate significant clustering [15,41]. In this study, the Q-value was 0.906, indicating the rationality of this network graph. The mean S-value was 0.95, wherein the S-values greater than 0.9275 for the #0 - #26 metacommunities indicate good homogeneity of these metacommunities. Table 5 lists the characteristics of the top 10 highly co-cited references related to glutamine metabolism in the field of diabetes, like Wise, D. R. et al. [42] in cluster #6 and Hensley, C. T. et al. [43], Son, J. et al. [44] and Gross, M. I. et al. [45] within cluster #9.

Furthermore, the timeline network map visualised the co-citations across different clusters, representing the evolution of knowledge in this research domain [16] (Fig. 5B). The bold timeline indicates that a cluster topic was a hot topic during a particular period. Tree rings of different sizes on the timeline represent high-quality articles with high citation frequency [49]. Moreover, in this research domain, stable isotope-resolved metabolomics has been a hotspot since 2006, peaking in 2012. L-glutamine surfaced as an emerging research field in 2011, garnering increased attention. Studies on glutamate dehydrogenase first appeared in 2002 and persisted over time. Notably, type 2 diabetes (cluster #7) surfaced as a recent, high-concern area, suggesting a critical role for Gln metabolism in diabetes progression.

3.6. Analysis of the most frequently occurring keywords

In addition to analysing references, the analysis of keywords also represents the core and thematic content of a particular subject

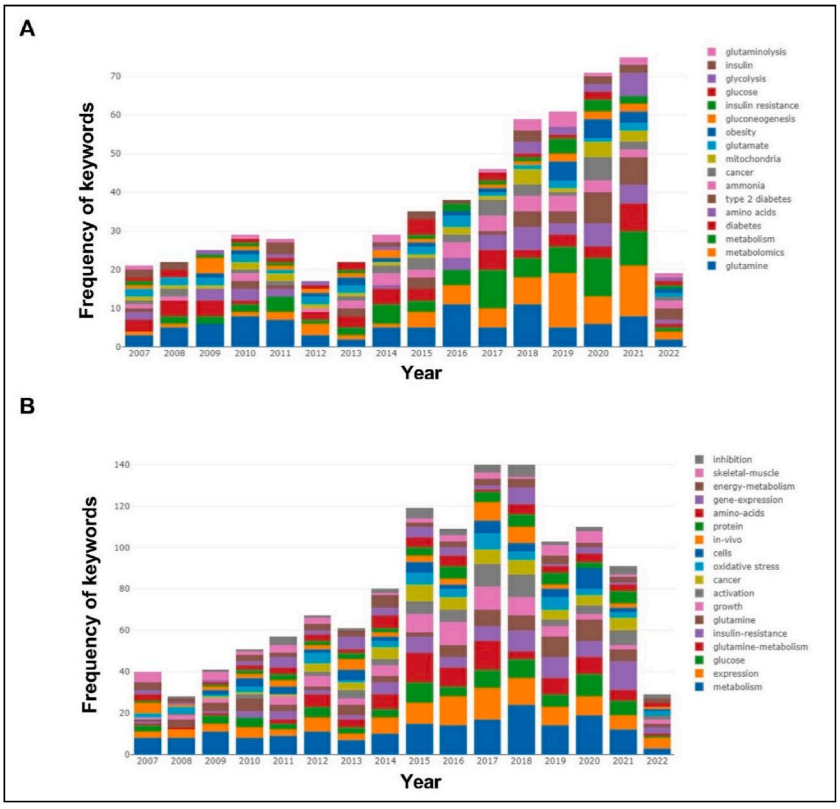

Fig. 7. Variation in the number of different keywords for research of diabetes and Gln metabolism AND diabetes and glutaminolysis from 2001 to 2022. **(A)** The bar chart of changes in the number of keywords. **(B)** The bar chart of changes in the number of keywords plus.

area, revealing field relevance and implied knowledge [50]. Another commonly used method for identifying hot research topics and areas is keyword co-occurrence analysis, which analyses research trends and development directions along with shifts in research trends and the emergence of novel issues within a particular knowledge domain. In this study, keyword clusters with a minimum of five occurrences were generated using the VOS viewer (Fig. 6A), wherein the size of each node represented the frequency of keyword occurrences. Four colors represented four different clusters. Clusters with common characteristics and attributes were classified into

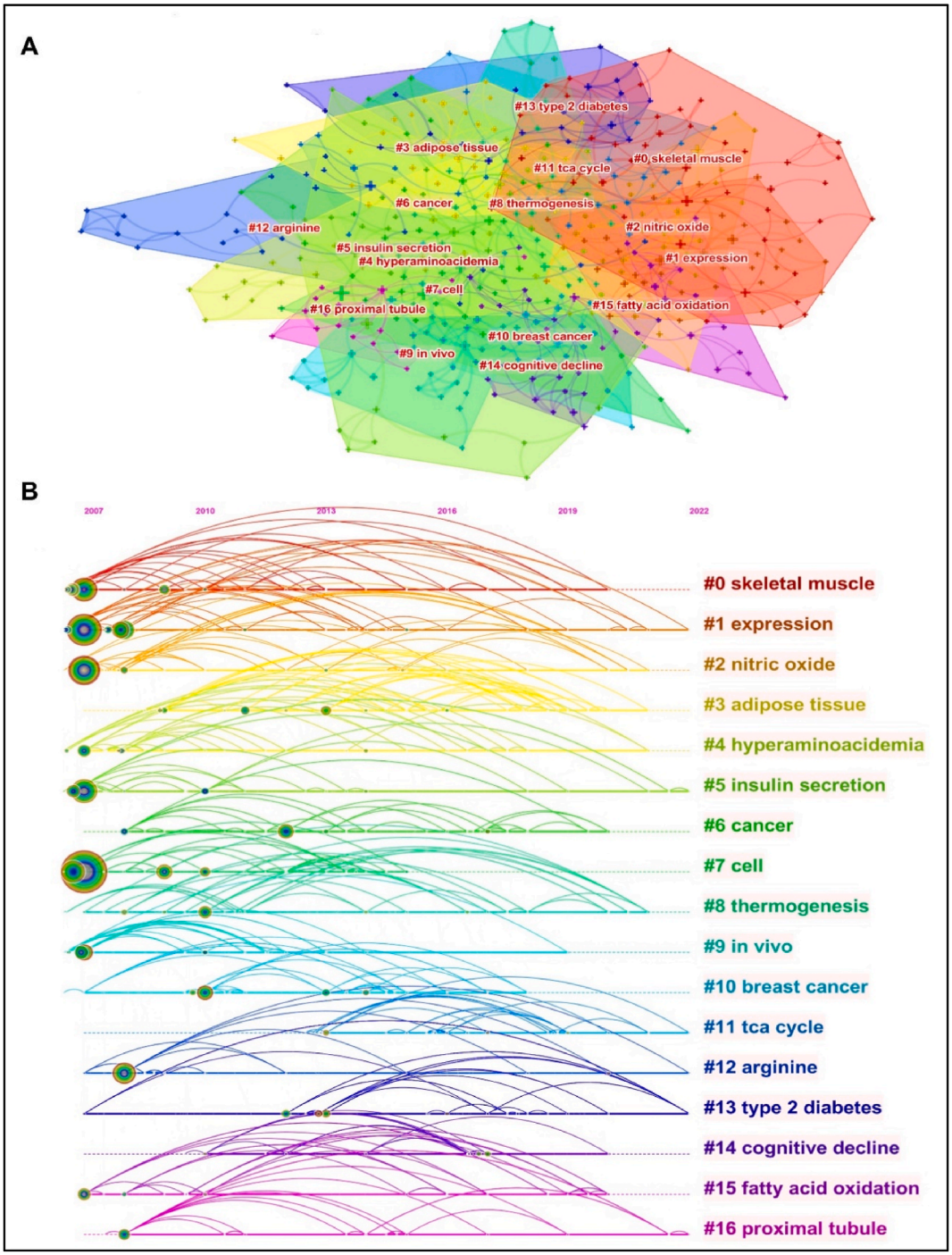

Fig. 8. Visualization map of keywords aggregation classification for diabetes and Gln metabolism AND diabetes and glutaminolysis research from 2001 to 2022. **(A)** Aggregated classification visualization of co-occurring keywords, divided into 17 clusters. Different colors represent clusters of different classifications. **(B)** Timeline visualization of co-occurring keywords. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

the same color-coded cluster, with green, blue, red and yellow clusters indicating association with 'glutamine plus glucose', 'glutamine metabolism', 'insulin resistance' and 'metabolism', respectively. After removing irrelevant keywords, we merged keywords with the same meaning. Fig. 6B provides an overlay visualization of the network map for the most frequent keywords in this field, where node size corresponds to keyword occurrence frequency, and node proximity indicates closeness of association. In addition to that, the thicker the line between two nodes, the more often they appear together. For example, in this study, 'metabolism' appeared the most, followed by 'glutamine'. The thick line between 'metabolism' and 'glutamine metabolism', 'cancer', 'diabetes' and 'obesity' indicates that they appear concurrently. To analyze the changes in the number of different keywords over the past 20 years and elucidate the relationship between different keywords, we used bibliometrics to generate a bar chart of the frequency distribution of keywords (Fig. 7A). Since 2007, the keywords 'glutamine', 'metabolomics' and 'diabetes' have been co-occurring at a high frequency in various studies. Moreover, the regulation of Gln metabolism plays a critical role in the progression of diabetes. Thus, further research and elucidation of these molecular mechanisms of Gln metabolism could facilitate the identification of new strategies for the treatment of diabetes. Notably, in the first half of 2022, the keywords 'glutamine', 'metabolomics', 'metabolism', 'diabetes' and 'type 2 diabetes' maintained high frequencies, highlighting their ongoing prominence in recent research. The bar chart of changes in the number of keywords over the past 20 years is displayed in Fig. 7B.

Furthermore, CiteSpace generated a landscape of keyword ensemble classes, presenting 17 ensemble swarm classes (Fig. 8A). The overlapping portion of the image indicated that this study has been cited in multiple clusters. Cluster #0, labelling the skeletal muscle, was the largest cluster, followed by expression (cluster #1) and nitric oxide (cluster #2). Apart from this, several research directions, including hyperaminoacidemia (cluster #4), insulin secretion (cluster #5) and cell (cluster #7), were highlighted and garnered attention from 2007 onwards. Meanwhile, TCA cycle (cluster #11), arginine (cluster #12) and type 2 diabetes (cluster #13) have been a research hotspot in this field. Furthermore, the co-occurrence keywords timeline graph is presented in Fig. 8B, which consists of 474 nodes and 1872 links.

3.7. Analysis of references and keywords using burst detection

Burst detection, a powerful tool that captures the sharp increases in reference or keyword popularity over time, is an algorithm developed by Kleinberg [51]. This analysis can effectively identify topics or concepts that have been discussed frequently over a period, as well as draw the attention of peer investigators to emerging concepts and future trends. The two properties of citation bursts are intensity and duration of state [16]. In our study, burst detection was used to extract key references and keywords. Using CiteSpace, the top 25 references with the strongest citation bursts from 2001 to 2022 are presented in Fig. 9. The blue represents the time interval, and the red represents the period of the reference burst. Among them, the strongest reference for burst value (strength: 10.78) was published in *Nature* by Metallo, CM et al. In this study, they found that the use and regulation of Gln metabolism in hypoxic cells, which identified a critical role for oxygen in regulating carbon use to produce Acetyl coenzyme A and support lipid synthesis in mammalian cells [32]. Furthermore, in 2007, the first burst of co-cited references commenced [52], peaking in 2020. A total of five references had a burst that lasted until 2022 [53–55]. The references with citation bursts between 2010 and 2020 accounted for 88.00 % of all bursts. Although the burst of most references has ended, the burst of some references continues, indicating that these research topics or key technologies have been receiving increasing attention recently.

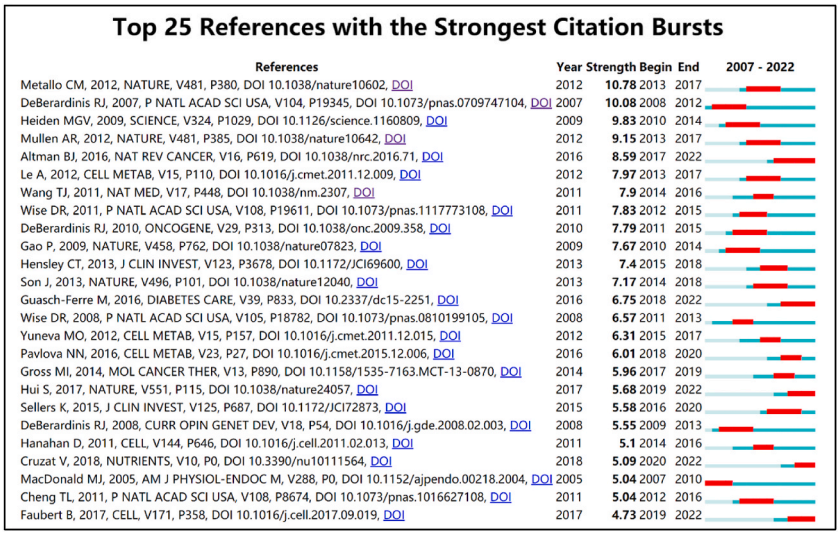

Fig. 9. The strongest burst strength citation of references on diabetes and Gln metabolism AND diabetes and glutaminolysis progression research between 2001 and 2022. The strength values reflect the frequency of citation. The red part indicates a sudden increase in the citation frequency of the reference during this time period. The blue segments represent relatively unpopular periods. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Detection and analysis of burst keywords represent the number of times keywords are cited frequently. Fig. 10 presents the top 25 keywords with citation bursts (with the red part representing the time interval of the burst). A stronger burst rate indicates more attention to the research topic. Over the years, 'type 2 diabetes' has ranked first with the highest burst strength (strength: 7.69), followed by 'proliferation' (strength: 5.01), 'transport' (strength: 4.89), 'rat brain' (strength: 4.31), and 'pancreatic beta cell' (strength: 4.16). Importantly, 'type 2 diabetes', 'risk', 'insulin sensitivity', 'tac cycle', 'individual', and prevalence became the focus in 2019, suggesting that these are current research hot topics.

4. Discussion

Diabetes, marked by hyperglycemia and hyperlipidemia due to impaired insulin secretion, insulin action, or both [12,56], has witnessed a global surge in morbidity and mortality, urging the pursuit of identifying possible therapeutic targets and novel clinical strategies [57]. As the knowledge of 'metabolism influences function' is further explored, Gln has been recognised as an essential amino acid involved in nucleotide biosynthesis, TCA cycle replenishment key, glutathione (GSH) and other non-essential amino acid synthesis [58,59]. Numerous studies have laid the groundwork for Gln metabolism and also provided new insights into the mechanisms of metabolic adaptation during tumor hypoxia [60,61], the emergence of drug resistance [62], mitochondrial glutamate metabolic reprogramming and y amidolysis-induced changes [63,64]. Yoo. HC et al., underscored the robust role of Gln in various biosynthesis, bioenergetics and adaptation to hypoxia based on compartmentalised Gln metabolism, emphasising its impact on cellular metabolic processes, including adaptation to hypoxia and epigenetic modifications [64]. Notably, discussions on Gln transporters have hinted at metabolic strategies targeting Gln metabolism in cancer cells [65]. Collectively, these findings illuminate Gln's extensive and critical role in complex cellular metabolism, offering promising avenues for intervening in various disease treatments.

However, can modulating Gln metabolism be a viable therapeutic strategy for diabetes? In-depth exploration and research validation remains imperative, This study utilised information visualization software to conduct a scientometric analysis of the literature on Gln metabolism in diabetes from 2001 to 2022. It systematically documented the field's evolution, context, hotspots and latest progress, offering researchers a macro-level grasp of future development. This review represents the first comprehensive systematic information on the association between Gln metabolism and diabetes through scientometric analysis and visual network mapping. Further exploration of Gln metabolism rules and mechanisms aims to delineate clear therapeutic targets and novel clinical strategies for diabetes and other diseases. We summarised four potential research fronts in Gln metabolism and diabetes as follows.

(1) Research on Gln metabolism in the field of diabetes has become an upward trend, but it is imperative to strengthen the cooperation between countries/regions or authors.

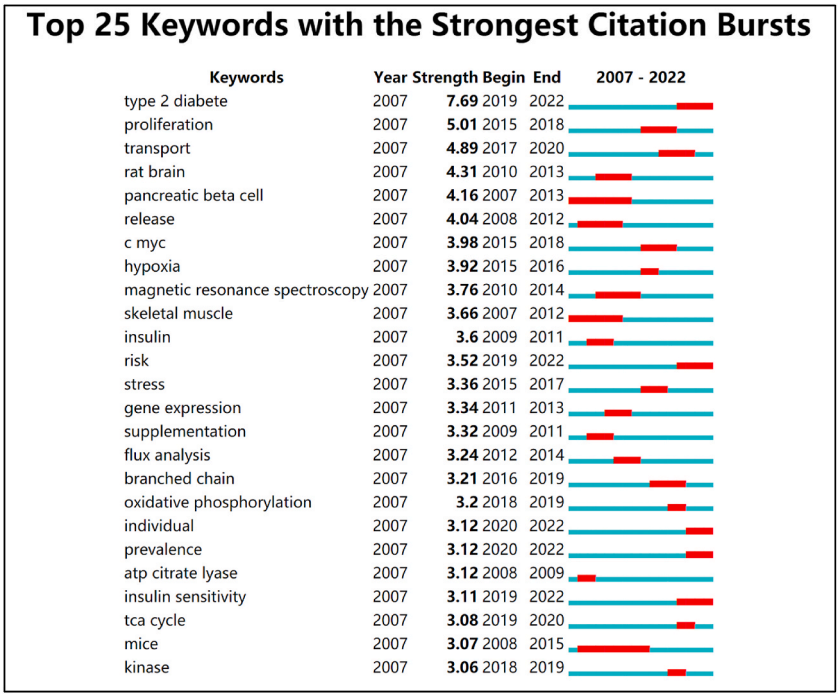

Fig. 10. The strongest burst strength citation of keywords on diabetes and Gln metabolism AND diabetes and glutaminolysis progression research between 2001 and 2022. The strength values reflect the frequency of citation. The red part indicates a sudden increase in the citation frequency of the keywords during this time period. The blue segments represent relatively unpopular periods. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Analysing the WoS database for Gln metabolism and diabetes-related articles from 2001 to 2022, we generated comprehensive, different-type maps. Quantitative and qualitative bibliometrics analysis using VOS viewer and CiteSpace software revealed the relationship between Gln metabolism and diabetes progression over the past 20 years. The number of research articles published has increased significantly, peaking at 85 articles in 2017. Moreover, the United States initiated this research and maintained steady growth, fostering substantial contributions and facilitating global cooperation. The development and level of scientific research in a country also reflect its comprehensive strength. Nonetheless, GDP disparities in scientific research allocation between countries underscore the need for enhanced communication between low- and middle-income countries and high-income countries. China, a developing country, has made tremendous progress in the number of publications in this domain since 2009. However, the top three research institutions with the most published results are all located in the United States, namely Vanderbilt University, Yale University and University of Texas Southwestern Medical Center at Dallas, remaining prominent in publication quantity, research quality and influence. Notably, researchers like Weiner, ID; Verlander, JW and Lee, HW has established robust collaborations, ranking second, fourth and sixth in the number of publications, respectively.

Summarising the above information, researchers can gain a better understanding of the development trends and future research directions in this field by consulting articles published by researchers in prolific countries or who closely cooperated. However, the cooperation between countries/regions and top researchers calls for further reinforcement. Efforts should prioritise fostering platforms for scholars to collaborate and communicate, fostering higher-quality publications in this domain.

(2) The integration and intersection of multidisciplinary provides cooperation strategies and technical guarantees for the development of this field.

Analysis of journals and co-cited journals serves as a compass for emerging researchers when selecting appropriate journals for submission [16,66]. Most of the relevant research articles within this domain were published in Q1 journals, encompassing globally influential publications like *Nature, Cell, Science, Cell Metabolism*, and *Journal of Clinical Investigation*. These outcomes underscore the pivotal role of regulating Gln metabolism in diabetes onset and progression, commanding the interest and attention of many researchers. Simultaneously, the identified research hotspots, challenges, value and significance have gained widespread acknowledgement among scholars.

Interestingly, the concordance rate between the top 10 co-cited journals and the top 10 most active journals is 50 %, which suggests that the quality of research in this field can be further improved by strengthening international cooperation among researchers and promoting close collaborations between institutions, providing strategies and guidelines for future research development. Additionally, existing literature in this field centres mainly on cell biology [67], microbiology [31], nutrition and physiology, molecular genetics, biochemistry molecular biology [68], endocrinology and other disciplines. This signifies a characteristic trait of research in this field: an intersection and integration of multidisciplinary approaches. Moreover, the interdisciplinary amalgamation across diverse domains stands to break through the technical barriers in Gln metabolism and diabetes research, furnishing cooperation strategies and technical support, thereby advancing the field's frontiers.

(3) The research consensus of 'metabolism affects function' has an unprecedented development prospect in this field.

The co-citation reference network showed that the top 10 highly co-cited references were predominately associated with theme cluster #0 (sirtuins) and theme cluster #3 (L-glutamine). Notably, theme cluster #1 (stable isotope-resolved metabolomics) emerged as a pivotal technique, enabling high-throughput analysis of metabolic status from a specimen (metabolomics). Among the top 10 co-cited references, the foremost was published by Professor Ralph J. DB's group in *Proceedings of the National Academy of Sciences* in 2007 [28], illuminating transformed cells increased Gln consumption and its facilitation of glucose-derived carbon utilisation and biosynthesis. This unveiled the mechanistic connection between 'metabolism' and 'cell growth control', with landmark implications for disease treatment. The subsequent significant co-cited reference was published by Matthew. G in *Science* in 2009 [29], proposed that the metabolism of virtually all proliferating cells, including cancer cells, can be adapted to facilitate the widespread uptake and infiltration of nutrients into the energy substances (such as amino acids, nucleotides and lipids) needed to generate new cells. It provided a new target for Gln metabolism in the treatment of cancer. Similarly, two other highly co-cited studies revealed a unique mechanism of Myc regulating Gln metabolising enzymes. These findings suggested that oncogenic levels of Myc induce a transcriptional programme that, by promoting Gln catabolism, triggers cellular addiction to Gln as a bioenergetic substrate [30,31], enabling a previously unanticipated link between Gln metabolism and energy homeostasis.

Of particular interest in cluster #7 (type 2 diabetes) was an article published by Prof. Thomas. JW's group in *Nature Medicine* in 2011 [34]. This study leveraged emerging technology-metabolomics to probe blood samples, predicting diabetes onset and progression. The expression of five branched-chain amino acids (isoleucine, leucine, valine, tyrosine and phenylalanine) was also significantly associated with future incidence of diabetes. These findings underscored the potential importance of amino acid metabolism in predicting the occurrence of diabetes and confirmed that further study of amino acid profiles can aid in assessing future diabetes risk. Additionally, Prof. Christopher. BN's group used metabolomic analysis to reveal the rules and characteristics of metabolites closely related to branched-chain amino acids (BCAAs) in obese and lean people. Their findings suggested that BCAAs contribute to the progression and development of obesity-related insulin resistance, even in the context of poor dietary patterns involving high-fat consumption [33].

Fig. 6, the keyword clustering diagram, delineates four clusters, interconnecting Gln, metabolism, and the crucial role of insulin resistance. The past two decades have witnessed substantial strides in uncovering insulin resistance and its significance in obesity,

diabetes and other related metabolic diseases [69]. While traditionally linked to type 2 diabetes [70,71], emerging evidence suggests its association with increased morbidity and mortality in type 1 diabetes [72]. Therefore more in-depth research is required to comprehensively understand the pathological and physiological characteristics of insulin resistance coexisting with other chronic diseases. A 2017 study that investigated the effects of insulin resistance on lipid metabolism and its products at the preclinical level revealed that strong predictors of lipoprotein dysfunction were quantitatively and qualitatively characterised by insulin resistance and diabetes, respectively [73]. Further in-depth research on related metabolic mechanisms revealed that metabolites represented by Gln and glutamate play a critical role in promoting the progression of diabetes and other chronic diseases [74,75]. In an article published in 2021, it was demonstrated that the induction and conversion of glutamate to α-KG regulates metabolic flux under normal physiological conditions. Moreover, it also revealed that dyslipidemia and insulin resistance started in the offspring of obese mothers. If these are not genetically linked, the metabolic disorder may be due to abnormal placental metabolism in the mother with potentially long-term adverse health effects on the health and well-being of the offspring [76]. Therefore, an in-depth exploration of Gln metabolism holds promise as an intriguing and novel therapeutic avenue for diabetes treatment.

(4) The study of Gln metabolism is still a frontier field and hot topic in the treatment of diabetes.

Analysis from CiteSpace software revealed the research trends in this domain that align with the oscillating nature of co-cited burst references. The first representative reference authored by Metallo, CM et al. emerged with the most sustained citation burst in the field with a strength of 10.78 [32]. The second highest reference (strength: 10.08) further clarifies that Gln metabolism can provide a carbon source, thereby promoting the ability of cells to use glucose-derived carbon and TCA cycle intermediates as biosynthetic precursors, setting the stage for exploring its impact on cellular function [28]. Citation burst analysis revealed that exploring the intricate mechanisms of Gln metabolism remains a popular topic in the treatment of diabetes. Additionally, the correlation between the two needs to be verified with the help of burgeoning research tools. Moreover, interdisciplinary integration and the advent of artificial intelligence technology will undoubtedly invigorate and propel research in this field.

Evaluating emergent keywords delineated the research into three distinct stages based on the start time and end time. The first stage included ‘pancreatic beta cell’, ‘skeletal muscle’, ‘atp citrate lyase’, ‘insulin’ and ‘supplementation’, hinting at metabolism’s broad recognition across diverse research domains. The second stage included ‘magnetic resonance spectroscopy’, ‘gene expression’, ‘flux analysis’, ‘proliferation’, ‘c-myc’, ‘hypoxia’, ‘branched chain’, ‘oxidative phosphorylation’ and ‘kinase’, confirming the beneficial effects of studying cellular function and various glucose and lipid metabolism disorders in disease pathogenesis, laying the groundwork for specific target and mechanism studies. Additionally, emerging research tools and methods have also made great contributions to the rapid development of this field. The third stage, commencing in 2019 and maintaining a certain intensity, specifically includes ‘type 2 diabetes’, ‘risk’, ‘insulin sensitivity’, ‘tca cycle’, ‘individual’, and ‘prevalence’. A growing body of literature supports the modulation of Gln metabolism and metabolites (glutamine, glutamate, α-KG) as promising avenues for diabetes treatment, aligned with the surge in keyword frequency observed in this study.

However, validating whether Gln metabolism can improve diabetes necessitates extensive clinical studies and basic experiments. To comprehend this complex relationship between Gln metabolism and diabetes, larger biological sample sizes representing diverse populations are required, accounting for various metabolites, emerging investigational drugs and novel therapeutic targets that could diabetes. Furthermore, leveraging emerging artificial intelligence techniques like high-throughput screening techniques and neural network deep learning will be instrumental in deciphering and extracting meaningful insights from the copious data generated by these studies.

5. Conclusion

Our knowledge and understanding of ‘metabolism affect function’ has been significantly improved through meticulous analysis of high-quality articles by previous researchers. The insights gleaned through CiteSpace enabled us to summarize the molecular mechanisms and research hotspots elucidating the impact of Gln metabolism on diabetes development (Fig. 11).

Our research unveiled a significant increase in global research on the regulation of Gln metabolism for diabetes treatment since 2007. This expanding field primarily revolves around the intertwined systems of ‘glutamine -metabolism’ and ‘type 2 diabetes’. The United States emerges as a trailblazer in this research domain, fostering international collaborations. However, strengthening cooperative efforts among countries/regions or authors remains imperative. Additionally, the convergence and interplay of multidisciplinary approaches offer strategies and technical guarantees for the development of this field. We anticipate that further in-depth exploration in this field will yield breakthroughs in discovering new glutamine metabolites, investigating emerging therapeutic drugs, identifying novel therapeutic targets or developing novel tools for the treatment of diabetes.

6. Strengths and limitations

To the best of our knowledge, this scientometric survey article is the first to identify and explore the association between Gln metabolism and diabetes development. Diverging from traditional narrative reviews, scientometrics offers explicit insights into frontier topics and research trends across diverse fields, facilitating new research directions and collaborative opportunities for scholars. However, our study has several limitations. Firstly, primarily reliant on the WoS database, our analysis might suffer from publication and citation reliability issues due to database constraints and language biases, limiting the comprehensiveness of research data. Secondly, to ensure the accuracy and research quality of all included literature analyses, we solely included reviews and articles

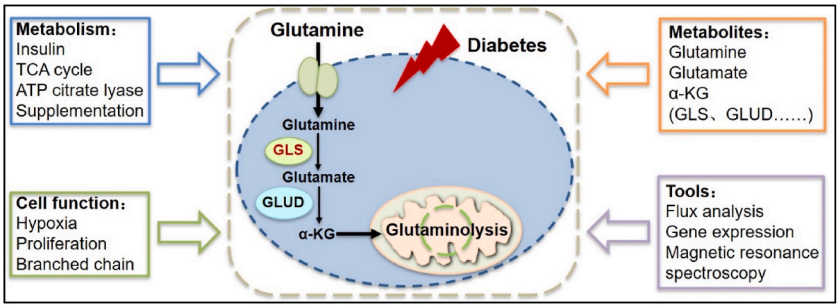

Fig. 11. Influence of Gln metabolism on diabetes development.

published in English, which adds another layer of potential bias. Thirdly, our selective analysis may overlook nuanced details. The potential for bias persists due to similarities in author names and initials, variations in keyword expressions and continuous database updates. For example, as shown in Fig. 6, certain synergistic keywords are similar and should be grouped in the same circle, such as 'diabetes' and 'type 2 diabetes', 'metabolism' and 'metabolomics'. Future studies might address these limitations more effectively.

Despite these methodological limitations, scientometrics remains a vital tool for evaluating research across various fields, spanning disease studies [77,78], natural medicine development [51,79], and emerging technologies [80,81]. Our study, despite its limitations, offers a diversified, global perspective on Gln metabolism's role in diabetes treatment and aims to serve as a representative study in this domain.

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Data availability statement

Data included in article/supp. Material/referenced in article.

CRediT authorship contribution statement

Meina Zhao: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Conceptualization. **Kaiyan Wang:** Writing – original draft, Methodology, Formal analysis. **Rui Lin:** Writing – review & editing, Validation, Supervision, Software, Resources. **Fei Mu:** Visualization, Resources, Investigation, Funding acquisition. **Jia Cui:** Methodology. **Xingru Tao:** Supervision, Software. **Yan Weng:** Visualization, Data curation. **Jingwen Wang:** Resources, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e25258.

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