Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2026;15(1):453-63

Tracking Irisin's cardiovascular footprint: A bibliometric analysis of global scientific activity (2012-2025)

Seher Nasircilar Ulker[1], Gunnur Kocer[2]

[1]*Alanya Alaaddin Keykubat University, Faculty of Health Sciences Department of Physiotherapy and Rehabilitation, Antalya, Türkiye*
[2]*Near East University, Faculty of Medicine, Department of Physiology, Nicosia, TRNC, Mersin 10, Türkiye*

Received 30 September 2025; Accepted 25 October 2025
Available online 27 February 2026 with doi: 10.5455/medscience.2025.09.259

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial-NonDerivatives 4.0 International License.

Abstract

Irisin, a myokine induced by exercise, is a key regulator of metabolic processes and cardiovascular health, has emerged as a potential biomarker and therapeutic target in cardiovascular disease. However, the global research landscape on this topic has not been systematically mapped. The aim of the study to provide a comprehensive bibliometric analysis of irisin-related cardiovascular research published between 2012 and 2025. Publications indexed in the Web of Science Core Collection were analysed using VOSviewer. Annual output, country- and institution-level productivity, co-authorship patterns, document citations, and author keyword co-occurrence were assessed. Annual output revealed a three-phase trajectory: rapid emergence (2012–2015), steady expansion (2016–2021), and recent volatility without contraction (2022–2025). China was the most prolific contributor (194 publications), followed by the United States (55), Türkiye (40) and Italy (34). Fırat University (Türkiye) and Southwest Medical University (China) were the most productive institutions, while Harvard University (USA) achieved the highest citation impact. Co-authorship analyses showed China and the United States as global anchors, though collaboration remained regionally clustered. Highly cited works by Pedersen (2012), Park (2013), and Perakakis (2017) served as conceptual anchors, with subsequent studies by Jedrychowski, Polyzos, Xiong, and Zhu consolidating the knowledge base. Keyword co-occurrence analysis positioned irisin as a central hub linking exercise physiology, metabolic disorders, and cardiovascular pathology, while overlay visualization showed a thematic shift from early mechanistic studies to cardiometabolic diseases and, most recently, cell-death pathways (pyroptosis, autophagy) and specialized clinical populations. In conclusion, irisin-related cardiovascular research has grown rapidly over the past decade, with China emerging as the dominant contributor and the United States maintaining strong collaborative reach. Thematic evolution reflects a trajectory from molecular mechanisms to clinical applications. Standardized methodologies and expanded multinational collaborations are needed to address existing gaps and advance irisin's translational potential in cardiovascular medicine.

Keywords: Bibliometric, cardiovascular, irisin, VOSviewer

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, presenting a substantial global health burden [1,2]. The intricate pathogenesis of CVDs involves a complex interplay of genetic, environmental, and lifestyle factors, often characterized by endothelial dysfunction, inflammation, oxidative stress, dyslipidemia, and metabolic derangements [1,3,4]. Understanding novel therapeutic targets and biomarkers for the prevention, diagnosis, and treatment of CVDs is therefore of paramount importance. Among such emerging candidates is irisin, a myokine first identified in 2012 by Boström et al., which is released from skeletal muscle during physical activity [5]. Irisin, initially identified in skeletal muscle, is also expressed in many different tissues, including the liver, brain, pancreas, kidney, gut, prostate, and ovary, heart and adipose tissue [6,7]. Exercise induced peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) expression, which triggers the production of fibronectin type III domain-containing protein 5 (FNDC5), leading to its cleavage and the release of irisin in several tissues [5,8].

Since its discovery, irisin has been recognized for its role in energy homeostasis, adipose tissue browning, and systemic metabolic

CITATION
Nasircilar Ulker S, Kocer G. Tracking Irisin's cardiovascular footprint: A bibliometric analysis of global scientific activity (2012-2025). Med Science. 2026;15(1):453-63.

Corresponding Author: Seher Nasircilar Ulker, Alanya Alaaddin Keykubat University, Faculty of Health Sciences Department of Physiotherapy and Rehabilitation, Antalya, Türkiye
Email: seher.ulker@alanya.edu.tr

DOI: 10.5455/medscience.202509.259

regulation [7]. Beyond these metabolic effects, accumulating evidence indicates that irisin exerts cardioprotective actions [9], such as reducing oxidative stress and inflammation, enhancing endothelial function, and mitigating myocardial fibrosis and remodeling [10,11]. These multifactorial roles have positioned irisin as a promising biomarker and potential therapeutic agent in cardiovascular medicine [6,12].

Bibliometric analysis offers a powerful methodology to quantitatively assess the intellectual structure, emerging trends, and collaborative networks within a specific field of research. By examining publication patterns, keyword frequencies, citation relationships, and author collaborations, bibliometric studies can illuminate the evolution and impact of scientific activity [13,14].

Recent bibliometric studies have already begun to map the irisin literature. A comprehensive analysis of Web of Science records (2012–2021) quantified publication growth, leading countries and institutions, prominent authors, and keyword clusters (noting hotspots such as insulin resistance, inflammation and circulating irisin measurements, and identifying prospective frontiers such as BDNF and osteoporosis) [15]. A more focused bibliometric study demonstrates the usefulness of discipline-specific mapping to reveal thematic concentrations and translational gaps [16]. However, despite the importance of irisin in cardiometabolic pathways [6,16-18], there are no comprehensive bibliometric studies focusing on its role in cardiovascular health and disease.

This study, therefore, employs bibliometric techniques to systematically explore the global scientific activity surrounding irisin in cardiovascular research over the past two decades. By mapping publication trends, identifying influential authors and institutions, and highlighting emerging research themes, this work aims to provide a comprehensive overview of how irisin's cardiovascular relevance has been shaped and where future investigations may be headed.

Material and Methods

Bibliometric analysis is widely recognised as a quantitative, science-mapping technique situated within the broader field of scientometrics. Rather than testing causal hypotheses, it systematically mines publication metadata—titles, abstracts, keywords, references and authorship information—to uncover the structural and evolutionary properties of a knowledge domain. In this respect it complements, but is methodologically distinct from, narrative or systematic literature reviews because it relies on objective counting rules and network-analytic algorithms to reveal latent patterns that may elude manual synthesis [14]. Recent methodological surveys further classify bibliometric mapping as an evidence-based tool for "research profiling," "intellectual structure" and "trend" analyses, making it especially suitable for disciplines that have expanded rapidly and in a dispersed manner [19]. The present study adopts this quantitative, exploratory paradigm to chart authorship networks, institutional linkages, citation backbones and thematic clusters, thereby providing a reproducible overview of irisin-related cardiovascular research that can guide future hypothesis-driven work [13].

To chart the intellectual landscape of irisin–cardiovascular research, bibliographic records were harvested exclusively from the Web of Science Core Collection because it provides uniform indexing standards and export formats that interface smoothly with VOSviewer. Data were extracted from the Web of Science Core collection on June 30, 2025. The topic search string:

TS=(("irisin" OR "FNDC5" OR "fibronectin type III domain containing 5") AND ("cardiovascular health" OR "cardiovascular disease" OR "cardiac disease"

- OR "heart disease" OR "vascular disease" OR "atherosclerosis"
- OR "hypertension" OR "myocardial infarction" OR "stroke"
- OR "heart failure" OR "coronary artery disease"
- OR "endothelial function" OR "cardiometabolic"))

returned 536 records for the period 2012 – 2025. WoS refinement filters were then applied in three steps:

1. Document type=Article or Review Article → 497 items
2. Language=English → 493 items

Complementary bibliometric techniques were performed with VOSviewer v1.6.20 to address the study's research purposes: (Table 1)

All networks employed VOSviewer's association-strength normalisation and default clustering algorithm. Node size denotes production (publications or occurrences), edge thickness represents relational strength (links or total link strength (TLS)), and colour encodes cluster membership; for the overlay map, colour instead reflects average publication year, thereby visualising temporal shifts in topic prominence.

Table 1. Bibliometric techniques with VOSviewer

Technique	Network unit	Purpose
Co-authorship	authors, organisations, countries	identify leading contributors and map collaboration architecture
Keyword co-occurrence	author keywords	trace conceptual structure and emerging themes over time (overlay visualisation)
Document citation	individual papers	detect seminal works and reveal the internal citation backbone

DOI: 10.5455/medscience.202509.259

Using a single database avoids cross-platform duplication but may omit items indexed elsewhere; the English-only filter likewise under-represents non-English output. Citation counts favour older papers, while 2025 data are partial. These constraints are acknowledged when interpreting productivity and impact metrics.

Result

Descriptive Information on Publications

Analysis of the annual output reveals a clear three-phase trajectory in the literature on irisin and cardiovascular disease (Figure 1). Phase I (2012–2015) is characterized by modest absolute numbers but a steep relative rise, with publications increasing from 3 in 2012 to 18 in 2015—an early four-fold expansion that reflects the field's emergence. Phase II (2016–2021) shows sustained, almost linear growth: output climbs from 26 to a pre-pandemic peak of 62 papers in 2021, representing more than a ten-fold increase over the 2012 baseline and signalling consolidation of irisin as a mainstream cardiometabolic research topic. Phase III (2022–2025) is marked by volatility rather than contraction. Production remains high in 2022 (≈60 articles), dips to 45 in 2023, rebounds to an all-time maximum of 65 in 2024. As of June 2025, a total of 33 articles have been published, indicating a lower current count compared to previous years; however, this may increase as the year progresses. The figure best interpreted cautiously, as it likely reflects partial-year indexing.

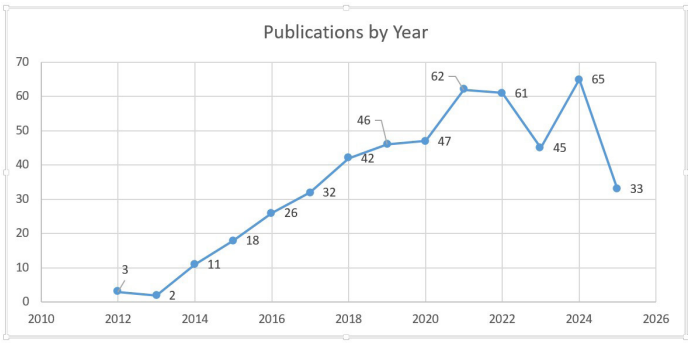

Figure 1. Publications by year

The country-level productivity data show a highly uneven distribution of output on the irisin–cardiovascular topic (Figure 2). The People's Republic of China is by far the principal contributor, accounting for 194 publications—more than three times the volume of any other nation. The United States follows at a distant second with 55 papers. US is followed by Türkiye with 40, and Italy with 34 articles, while Spain (22) and Poland (21) occupy the upper end of the middle range. Further down the list, Iran (20), Brazil, Egypt and Ukraine (18 each) share similar levels of activity, with Canada (16), South Korea (15) and Austria (15) also maintaining a visible presence. Output then tails off gradually across Japan, Greece, Switzerland, Germany and several countries.

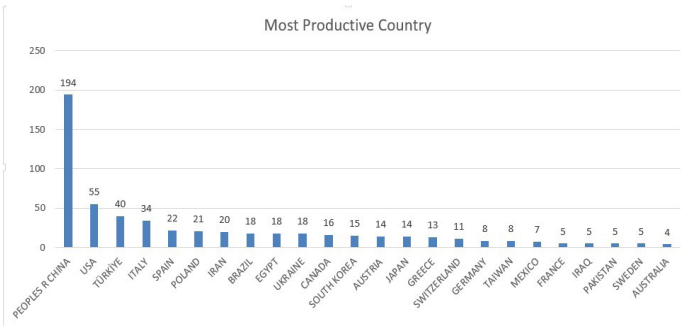

Figure 2. Most productive countries

Based on the institutional productivity chart (Figure 3), Fırat University School of Medicine heads the field with 10 publications on the irisin–cardiovascular nexus. It is followed by The Affiliated Hospital of Southwest Medical University with eight papers, and a cluster of Chinese institutions—Nanjing Medical University, its affiliated Faculty of Medicine, and Xijing Hospital—each contributing seven articles. Mid-tier output (six papers apiece) is recorded by the Army Medical Center of the PLA and the National and Kapodistrian University of Athens, while Shanghai Medical University, Xiangya Hospital (Central South University) and Zhongnan Hospital round out the top group with five publications each.

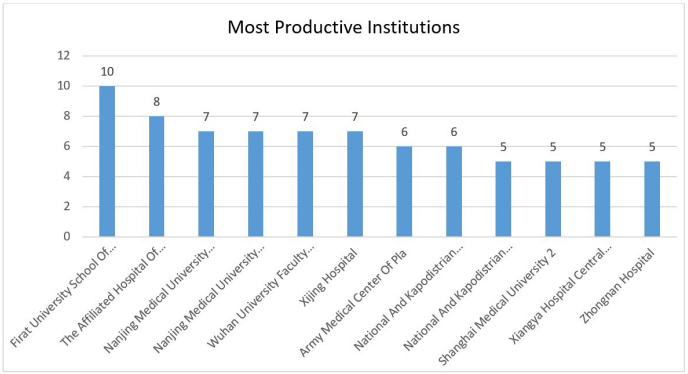

Figure 3. Most productive institutions

Co-authorship Analysis– Authors

In the author-level co-authorship analysis, 1 000 authors were initially screened under the minimal criteria of at least one publication and one citation. VOSviewer identified a largest connected component comprising 71 authors; Table 2 lists the ten most prominent members of this component. Kang Yu-Ming and Zhu Guo-Qing head the network with identical publication and citation counts and share the highest TLS (85), marking them as central collaborators whose work is frequently co-attributed with many peers. Chen Qi and Li Yue-Hua follow closely, each with seven papers, 359 citations, and strong collaborative footprints (TLS=72). Alejandro Lucia, despite a lower citation

DOI: 10.5455/medscience.202509.259

tally, exhibits a notable TLS (65), reflecting extensive partnership breadth relative to output volume.

Dominating the left half of the co-authorship network (Figure 4) is a densely knit green cluster led by Kang Yu-Ming, whose node acts as both the local and global hub: Kang links a core of frequent collaborators (e.g., Chen Qi, Li Yue-Hua, Zhou Hong) with a peripheral blue satellite cluster of junior colleagues (including Li Ying, Liu Yu) that appears almost exclusively connected to the field through Kang's group. Extending outward from the green core, Chen Dan forms the strategic bridge to a yellow cluster centered on Jiang Pei, Han Wenxiu and Guo Yujin; the thick bidirectional links underscore sustained, multi-author collaborations rather than occasional co-authorships. At the far right, an insular yet tightly woven red cluster anchored by Zeng Chun-Yan and Zhang Jun exhibits intense internal collaboration but relatively few ties to the broader network—its principal point of articulation being a single conduit through the Jiang–Chen Dan bridge.

Table 2. Top 10 authors in the co-authorship network on irisin and cardiovascular research, (thresholds:≥1 document,≥1 citation; largest connected component=71 authors)

Rank	Author	Documents	Citations	Total Link Strength*
1	Kang, Yu-Ming	8	392	85
2	Zhu, Guo-Qing	8	392	85
3	Chen, Qi	7	359	72
4	Li, Yue-Hua	7	359	72
5	Lucia, Alejandro	6	197	65
6	Jiang, Wei	4	224	63
7	Tao, Ling	4	277	50
8	Yan, Wenjun	4	277	50
9	Li, He	3	198	49
10	Berezin, Alexander E.	14	122	47

*Total Link Strength (TLS) sums all co-authorship links an author shares with the other 70 authors in the main component; higher values denote broader collaborative reach

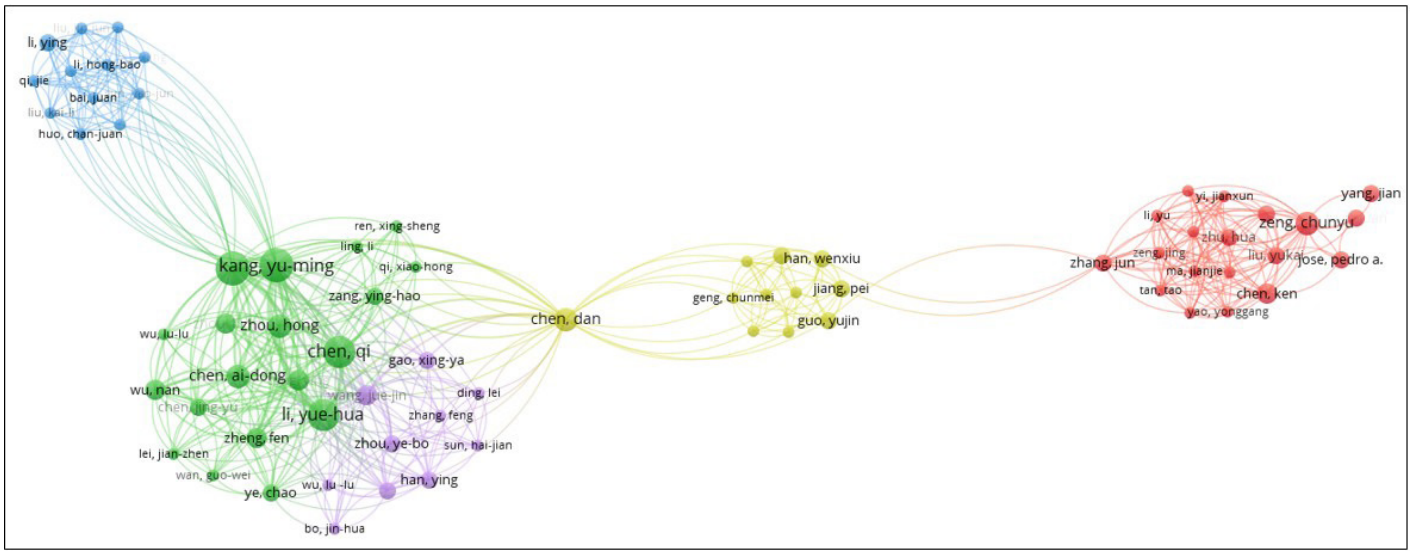

Figure 4. Co-authorship – authors

DOI: 10.5455/medscience.202509.259

Co-authorship Analysis –Organizations

The organisation-level co-authorship analysis (Table 3) examines how research institutions collaborate within the 493-article corpus. Each node represents an organisation, sized by its publication output, while inter-institutional links denote joint author affiliations on the same papers. Applying minimal inclusion thresholds yielded 763 institutions, of which 302 form the largest connected component visualised. The co-authorship map at the organisation level depicts a linear "chain" of institutional clusters that links regional hubs across three continents (Figure 5). On the far left, Fırat University forms the largest and most intensely coloured red node, signalling both the highest publication volume and the strongest collaborative pull within the network. Directly connected to it is University of Palermo, whose similarly large pink node functions as the primary European bridge, channelling co-authorship ties from Mediterranean partners (e.g., Buzzi Children's Hospital) toward Asian institutions. Mid-chain, illustrating Asia–Europe linkages that remain relatively modest in breadth but crucial for network continuity. A pronounced blue cluster emerges to the right, dominated by Xi'an Jiaotong University, Capital Medical University, and Southwest Medical University. Smaller green nodes in this region—such as Tianjin Medical University and Boston University—suggest targeted joint projects rather than wide-ranging partnerships. At the extreme right, a constellation of grey and light-green nodes—Harvard University, Harvard Medical School, Isfahan University of Medical Sciences—marks a second trans-regional anchoring point. Although Harvard's node is smaller than Fırat's, its position at the chain terminus and its multiple linkages underscore its role as the principal North-American gateway into the collaboration network.

Table 3. Top-ranked organisations in the co-authorship network on irisin–cardiovascular research, (thresholds:≥1 document,≥1 citation; largest connected component=302 organisations)

Rank	Organisation	Documents	Citations	Total Link Strength*
1	Fırat University	14	639	33
2	Harvard University	8	1 528	27
3	China Institute of Sport Science	3	107	26
4	European University of Madrid	3	107	26
5	Harvard Medical School	5	711	26
6	Keio University	3	30	24
7	Paracelsus Medical University Salzburg	8	116	24
8	University of Alcalá	3	96	24
9	Zaporizhzhia Medical Academy of Post. Edu.	7	67	24
10	Hospital Universitario 12 de Octubre	2	15	22

* Total Link Strength sums all co-authorship links an organisation shares with other institutions inside the 302-node component; higher values indicate broader collaborative reach

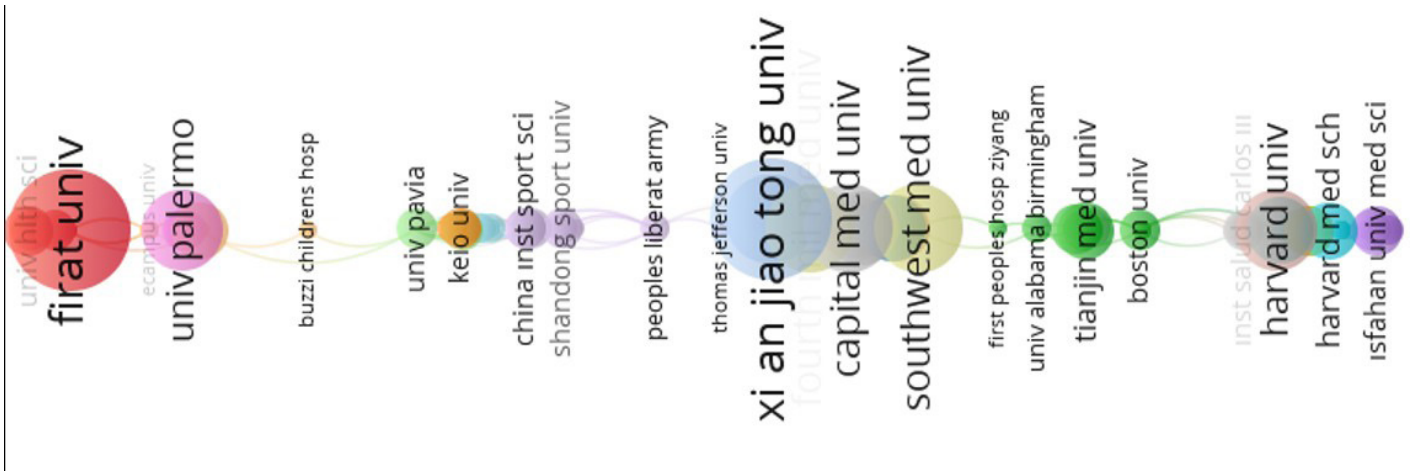

Figure 5. Co-authorship – organizations

DOI: 10.5455/medscience.202509.259

Co-authorship Analysis –Countries

The country-level co-authorship analysis (Table 4) covers 49 publishing nations and shows that 38 of them form one connected collaboration network. Within this network, the United States records the highest collaborative reach (TLS=52) and a substantial number of publications (55) and citations (4 054). China contributes the largest volume of papers (194) and total citations (5 558) and also collaborates widely (TLS=35). A group of European countries—Austria, Switzerland, and Ukraine—share similar TLS values of 24, indicating frequent cooperation within a regional cluster, even though their publication counts are comparatively modest. Canada and Spain achieve strong citation totals relative to their article numbers, while Italy, Germany, and Japan display balanced profiles in terms of publications, citations, and collaboration links.

Table 4. Leading countries in the co-authorship network for irisin-cardiovascular research, (thresholds:≥1 document,≥1 citation; largest connected component=38 countries)

Rank	Country	Documents	Citations	Link Strength*
1	USA	55	4 054	52
2	People's Republic of China	194	5 558	35
3	Austria	14	129	24
4	Switzerland	11	60	24
5	Ukraine	18	135	17
6	Canada	16	693	17
7	Spain	22	1 174	16
8	Italy	34	833	14
9	Germany	8	680	13
10	Japan	14	309	13

* Link Strength is VOSviewer's aggregated measure of the number of distinct international co-authorship ties a country maintains within the main 38-country component; higher values indicate broader or more intensive collaboration

Citation Analysis of Documents

The document-level citation analysis delineates the internal citation structure of the 493-article corpus. For each publication the analysis records (a) the number of times it is cited by other items within the same dataset and (b) its Link value—that is, the count of distinct, direct citation connections it shares with peer articles. Pedersen (2012) [20] stands out as a foundational reference with more than 2 000 citations, yet its relatively modest link count (33) suggests that it is widely cited across subfields rather than densely coupled to a specific cluster of papers. In contrast, Park (2013) [21] and Perakakis (2017) [22] combine high citation totals with some of the largest link values (64 and 61, respectively), indicating that they not only attract broad attention but also sit at the centre of tightly knit bibliographic-coupling webs—functioning as conceptual anchors for subsequent research. The presence of several 2015–2018 papers (e.g., Jedrychowski, Polyzos, Xiong, Zhu) [11,23-25] shows that pivotal contributions continued well beyond the initial discovery period, reflecting an expanding and still-active knowledge base (Table 5).

Co-occurrence of Author Keywords

Co-occurrence analysis confirms irisin as the central topic in the field (303 mentions; TLS=462). Myokine (43; TLS=114) and FNDC5 (40; TLS=83) define irisin's molecular identity, while exercise (48; TLS=92) and obesity (32; TLS=76) concepts address lifestyle and metabolic aspects. Terms like insulin resistance (20; TLS=52) and metabolic syndrome (21; TLS=49) further support this. Clinically, cardiovascular disease (26; TLS=67), inflammation (24; TLS=57), and biomarker (30; TLS=56) point to irisin's diagnostic and therapeutic potential (Table 6).

The author-keyword co-occurrence map (Figure 6) identifies irisin as the central hub connecting all research themes. One cluster links exercise, skeletal muscle, and signalling pathways (e.g., AMPK, BDNF), reflecting the molecular mechanisms by which muscle activity raises irisin levels. Another cluster highlights irisin's metabolic role through associations with obesity, metabolic syndrome, and insulin resistance, while a sub-cluster positions it among myokines and adipokines. A major group of terms connects irisin to vascular pathology, including atherosclerosis, hypertension, myocardial infarction, and cardiovascular disease, closely tied to inflammation and oxidative stress. Peripheral nodes such as heart failure, type 2 diabetes, chronic kidney disease, and sarcopenia represent expanding clinical applications, while pyroptosis emerges as a consistent mechanistic focus.

DOI: 10.5455/medscience.202509.259

Table 5. Top 10 Most-cited documents in the irisin–cardiovascular corpus (Threshold ≥10 Citations; Largest Connected Set=234 Items)

Rank	Document (First author, year)	Citations	Links*
1	Pedersen (2012)	2 008	33
2	Perakakis (2017)	443	61
3	Jedrychowski (2015)	424	37
4	Park (2013)	407	64
5	Li (2017a)	231	39
6	Polyzos (2018a)	191	41
7	Xiong (2015)	184	32
8	Zhu (2015)	180	49
9	Lecker (2012)	179	30
10	Lu (2015)	178	58

"Links" denotes the number of bibliographic-coupling connections that each document shares with other items in the network. The minimum citation threshold was set at 10; 234 papers met this criterion, forming the largest set of connected items from which the 10 most-cited documents are shown here

Table 6. Top 10 Author-keywords in irisin–cardiovascular research (2012-2025) Identified by a VOSviewer Co-occurrence Analysis

Rank	Keyword	Occurrences	Total Link Strength
1	irisin	303	462
2	myokine	43	114
3	exercise	48	92
4	Fndc5	40	83
5	obesity	32	76
6	cardiovascular disease	26	67
7	adipokine	19	58
8	Inflammation	24	57
9	biomarker	30	56
10	Insulin resistance	20	52

The table lists the author-keywords that met the threshold of ≥ 5 occurrences (n =52); only the 10 highest-ranking terms are shown. "Total Link Strength" (TLS) is VOSviewer's metric summarising the cumulative co-occurrence links a keyword shares with all other keywords in the network

The overlay visualization (2012–2025) shows how research on irisin and cardiovascular health has evolved (Figure 7). Early work (2015–2018, dark green) focused on irisin's link to exercise, skeletal muscle, and metabolic control, establishing its role as a myokine derived from FNDC5. Later studies (2019–2021, light green) expanded to cardiometabolic conditions such as obesity, hypertension, and atherosclerosis, while highlighting irisin's potential as a biomarker and its involvement in inflammation, oxidative stress, and myocardial infarction. Most recent research (2022–2025, yellow) explores cell death pathways (pyroptosis, autophagy), immune regulation (neuroinflammation), and specific clinical populations (peritoneal dialysis, sarcopenia, children).

DOI: 10.5455/medscience.202509.259

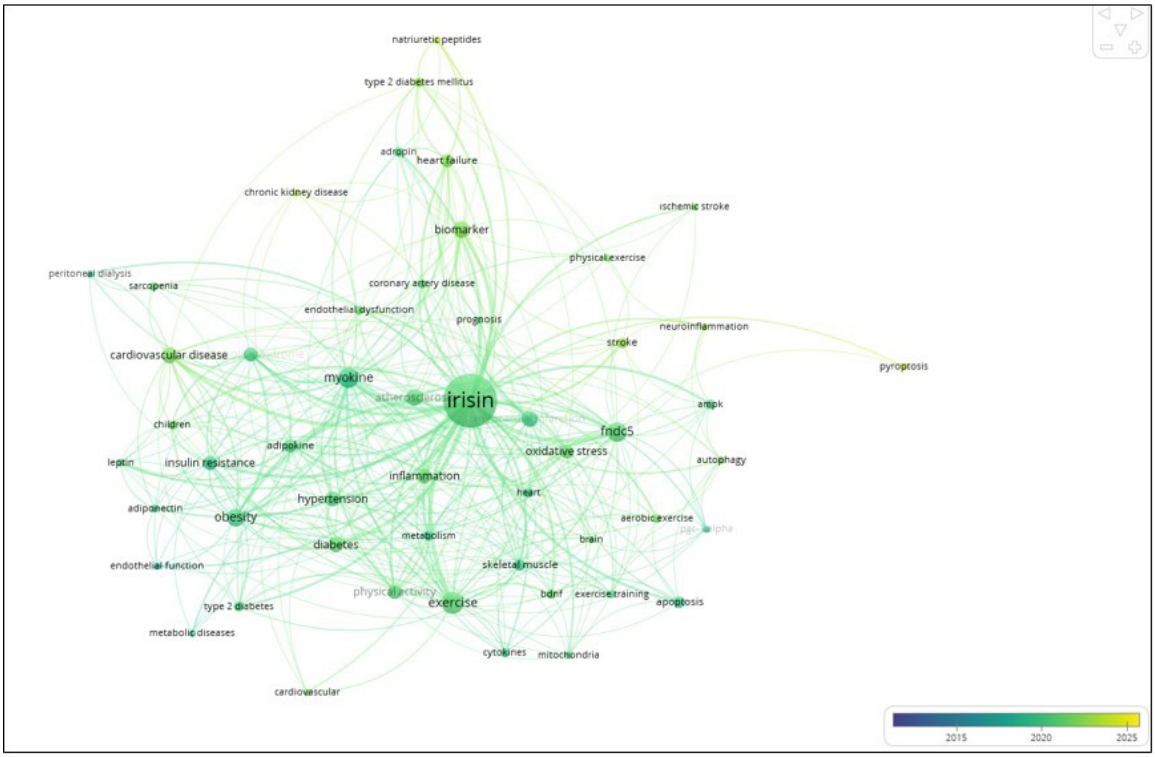

Figure 7. Overlay visualization of trend topics over time (2012-2025)

Discussion

This bibliometric analysis demonstrates that research on irisin and cardiovascular disease has developed along a three-phase trajectory, moving from early emergence through steady expansion to recent volatility, while maintaining high overall productivity. China has established clear leadership in publication output, with the United States, Italy, and Türkiye also making substantial contributions, and institutions such as Fırat University and Southwest Medical University acting as major hubs. Co-authorship analyses highlight strong national clusters anchored by China and the United States but reveal limited cross-regional integration. Citation mapping underscores the foundational influence of early works by Pedersen, Park, and Perakakis, while keyword analysis shows a thematic progression from molecular mechanisms and exercise physiology to cardiometabolic disorders, vascular pathology, and most recently, cell-death pathways and specialized patient populations.

Irisin, a myokine induced by exercise and produced by cleaving FNDC5, has been increasingly recognized for its cardioprotective potential [9] . Evidence suggests that it plays roles in endothelial function, vascular aging, hypertension, atherosclerosis, myocardial infarction, and heart failure [6,26]. Irisin enhances endothelial nitric oxide (NO) production, improving vasodilation and reducing endothelial dysfunction, which benefits patients with cardiovascular diseases like hypertension and atherosclerosis. Zhu et al. demonstrated that irisin rescues diabetic cardiac microvascular injury through suppression of oxidative stress [27]. Similarly, Chi et al. showed that irisin-enriched extracellular vesicles delay vascular aging by stabilizing sirtuin 6 (SIRT6), a key regulator of endothelial senescence [28]. Irisin also counteracts pathological vascular remodeling. Wang et al. reported that irisin alleviates vascular calcification by inhibiting vascular smooth muscle cell osteogenic differentiation and mitochondrial dysfunction [29,30]. Furthermore, irisin reduces arterial stiffness and improves vascular relaxation, which contributes to lowering blood pressure in hypertensive models [31,32]. Experimental models suggest that irisin exerts direct myocardial protection. Qin et al. reported that irisin is an effector in exercise-mediated rehabilitation after myocardial infarction, improving cardiac recovery [33]. Likewise, Lu et al. demonstrated that irisin decreases myocardial fibrosis and enhance cardiac function and infarct size [34]. Clinical research has shown that a higher risk of cardiovascular disorders such as heart failure and coronary artery disease is linked to decreased levels of irisin [35,36].

The emerging evidence on irisin's cardiovascular effects underscores the need to systematically map the research landscape in this field. Bibliometric analysis can accelerate the transition of irisin research from experimental promise to clinical application, ensuring efficient use of scientific resources.

When the distribution of annual publications is examined, the data depict a maturing field that, after a decade of uninterrupted

DOI: 10.5455/medscience.202509.259

expansion, has entered a period of cyclical fluctuation yet continues to generate a substantial volume of research each year. An analysis of country-level productivity data show that, although research is geographically widespread, it is predominantly driven by Chinese laboratories, with significant but significantly smaller contributions from the United States and a group of European and Middle Eastern countries. Also, Fırat University (Türkiye) and Southwest Medical University (China) were the most productive institutions, while Harvard University had a disproportionately high citation impact. The present bibliometric analysis highlights the rapid growth and evolving focus of irisin-related cardiovascular research. Our data demonstrate with China emerging as the leading contributor, consistent with earlier bibliometric mapping of global irisin studies which also identified China, the United States, and Türkiye as dominant contributors [15]. This pattern underscores both the international relevance of irisin and the persistence of regional research clusters, particularly between Asian and Western institutions.

In the co-authorship – author analysis, each node represents an author, its size reflects publication output, and the connecting edges indicate joint authorship ties; the accompanying Link or Total Link Strength metrics quantify the breadth and intensity of those ties. By visualizing these interactions, the analysis identifies tightly knit research teams, bridging scholars who connect otherwise separate groups, and peripheral contributors. Overall, the map portrays a collaborative landscape dominated by one highly integrative team that scaffolds several satellite groups, with only limited cross-talk occurring between the Kang-centered sphere and the more isolated Zeng-led cluster.

Co-Authorship analysis –organizations link counts quantify the breadth of an institution's collaborative reach, highlighting regional hubs, trans-continental bridges, and peripheral contributors. This network perspective thus complements the author-level findings by revealing the institutional architecture that underpins the field's knowledge production. Overall, the visual conveys a collaboration landscape that is neither fully centralized nor fragmented, but rather articulated through a succession of regional hubs whose bilateral ties create a single continuous pathway of knowledge exchange from Türkiye through Europe and East Asia to the United States. Moreover, the country-level co-authorship analysis point to active international partnerships centered on the United States and China, supported by well-connected European contributors and additional links from Canada, Japan, and other countries that together sustain global progress in irisin-related cardiovascular research.

Citation frequency signals an individual work's scholarly prominence inside the corpus, while the Link metric indicates the breadth of its bibliographic reach, identifying papers that act as connective hubs across thematic boundaries. Taken together, these two indicators provide a nuanced portrait of both intellectual influence and structural cohesion within the field. The fact that 234 documents are interlinked above the 10-citation threshold underscores a robustly connected literature, while the steep drop-off in citation counts after the top tier suggests a classic "long-tail" distribution in which a handful of landmark studies drive much of the field's scholarly momentum.

Irisin is a critical keyword for understanding the knowledge structure and of research trends in exercise-regulated myokines, playing a central role in identifying future research hotspots. From a bibliometric perspective, irisin stands out as a highly significant and frequently researched keyword within the field of exercise-regulated myokines. Its presence among the top keywords, alongside terms like "exercise" and "skeletal muscle," underscores its central role [37]. The keyword landscape of the current study represents a multidimensional research structure where irisin is found at the intersection of exercise physiology, metabolic regulation, and cardiovascular pathology. The co-existence of mechanistic terms (FNDC5, myokine), lifestyle (exercise, obesity) and clinical outcome (cardiovascular disease, biomarker) illustrates the translational course of the field. The fact that this pattern has developed indicates that the discovery of irisin has progressed beyond the discovery phase and has now started to be investigated both as a biological mechanism and as a clinical tool for cardiometabolic health.

The keyword co-occurrence map depicts irisin as hub of the discourse, its large red node radiating thick links to every colour cluster and confirming that virtually all thematic threads intersect through this peptide. A crimson cluster in the lower half binds exercise, skeletal muscle, PGC-1α, autophagy and signaling terms such as adenosine monophosphate-activated protein kinase (AMPK) and brain-drived neurotrophic factor (BDNF), illustrating the molecular cascade by which muscular activity elevates circulating irisin. At the right, a green cluster anchored by obesity, metabolic syndrome and insulin resistance underscores irisin's metabolic dimension, while a cyan sub-cluster centered on myokine and adipokine highlights its classification within the broader family of muscle- and fat-derived cytokines. Vascular pathology dominates the blue–purple band that arcs across the mid-map: nodes for atherosclerosis, hypertension, myocardial infarction and cardiovascular disease are densely inter-linked, and connecting edges to inflammation and oxidative stress emphasize shared mechanistic pathways. Heart failure, type 2 diabetes mellitus, chronic kidney disease and sarcopenia, as peripheral yellow nodes, have become a significant clinical frontier in the recent years, whereas the interdisciplinary concept of pyroptosis has persistently retained its lonely but closely knit posture in the same arena. Taken together, these lines of development trace the evolution of exercise physiology into a broad-based study of metabolic and cardiovascular pathology, and inflammatory pathways are critical bridges linking the separate clusters of knowledge into one coherent, multidimensional knowledge network.

The result of early studies (2015–2018) primarily focused on exercise physiology, skeletal muscle, and metabolic control, building the mechanistic framework that established irisin as a

DOI: 10.5455/medscience.202509.259

myokine derived from FNDC5 and linking it to physical activity. In the next phase (2019–2021), research broadened toward cardiometabolic conditions such as obesity, metabolic syndrome, hypertension, and atherosclerosis. At the same time, the idea of irisin as a biomarker became prominent, reflecting efforts to explore its diagnostic and prognostic value. The appearance of terms like inflammation, oxidative stress, and myocardial infarction further demonstrated growing interest in irisin's role in vascular injury and systemic stress. The most recent period (2022–2025) highlights emerging directions. Keywords such as pyroptosis, autophagy, and neuroinflammation point to deeper exploration of irisin's role in cell death and immune-modulatory mechanisms, while terms like peritoneal dialysis, sarcopenia, and children indicate a diversification toward specific patient populations and clinical contexts. Altogether, the field has evolved from early mechanistic studies to broader clinical research solidifying irisin's role in cardiovascular science.

Conclusion

In conclusion, irisin-related cardiovascular research expanded rapidly, with China as the leading contributor and the United States as the main collaborative center. The field shows a thematic progression towards cardiometabolic disorders, vascular pathology, and more recently, cell death pathways and specific patient populations, thus transitioning from mechanistic studies to clinical applications. Future progress will depend on assay standardization, large-scale validation, and strengthened multinational collaboration in cardiovascular medicine.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The bibliometric analysis used in this study was based on publicly accessible data from the open-access Web of Science database. Therefore, ethical committee approval was not required.

References

1. Jagannathan R, Patel SA, Ali MK, Narayan KMV. Global updates on cardiovascular disease mortality trends and attribution of traditional risk factors. Curr Diab Rep. 2019;19:44.
2. Di Cesare M, Perel P, Taylor S, et al. The heart of the world. Glob Heart. 2024;19:11.
3. Global Cardiovascular Risk C, Magnussen C, Ojeda FM, et al. Global effect of modifiable risk factors on cardiovascular disease and mortality. N Engl J Med. 2023;389:1273-85.
4. Shaito A, Aramouni K, Assaf R, et al. Oxidative stress-induced endothelial dysfunction in cardiovascular diseases. Front Biosci (Landmark Ed). 2022;27:105.
5. Bostrom P, Wu J, Jedrychowski MP, et al. A PGC1-alpha-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012;481:463-8.
6. Grzeszczuk M, Dzięgiel P, Nowińska K. The Role of FNDC5/Irisin in Cardiovascular Disease. Cells. 2024;13:277.
7. Mohammed SN, Jasim MH, Mahmood SH, et al. The role of irisin in exercise-induced muscle and metabolic health: a narrative review. Naunyn Schmiedebergs Arch Pharmacol. 2025;398:11463-91.
8. Paoletti I, Coccurello R. Irisin: A multifaceted hormone bridging exercise and disease pathophysiology. Int J Mol Sci. 2024;25:13480.
9. Ma C, Ding H, Deng Y, et al. Irisin: A new code uncover the relationship of skeletal muscle and cardiovascular health during exercise. Front Physiol. 2021;12:620608.
10. Zhao YT, Wang J, Yano N, et al. Irisin promotes cardiac progenitor cell-induced myocardial repair and functional improvement in infarcted heart. J Cell Physiol. 2019;234:1671-81.
11. Zhu D, Wang H, Zhang J, et al. Irisin improves endothelial function in type 2 diabetes through reducing oxidative/nitrative stresses. J Mol Cell Cardiol. 2015;87:138-47.
12. Fu J, Li F, Tang Y, et al. The emerging role of irisin in cardiovascular diseases. J Am Heart Assoc. 2021;10:e022453.
13. Aria M, Cuccurullo C. bibliometrix: an r-tool for comprehensive science mapping analysis. J Informetr. 2017;11:959-75.
14. Zupic I, Cater T. Bibliometric methods in management and organization. Organ Res Methods. 2015;18:429-72.
15. Liu J, Qi B, Gan L, et al. A bibliometric analysis of the literature on irisin from 2012-2021. Int J Environ Res Public Health. 2022;19:6153.
16. Wang J, Liu J, Pang W, et al. Research hotspots of irisin in the nervous system: a bibliometric study and visualization analysis via CiteSpace. Front Aging Neurosci. 2025;17:1488559.
17. Ho MY, Wang CY. Role of irisin in myocardial infarction, heart failure, and cardiac hypertrophy. Cells. 2021;10:2103.
18. Laurindo LF, Rodrigues VD, Laurindo LF, et al. Targeting AMPK with Irisin: Implications for metabolic disorders, cardiovascular health, and inflammatory conditions - A systematic review. Life Sci. 2025;360:123230.
19. Donthu N, Kumar S, Mukherjee D, et al. How to conduct a bibliometric analysis: An overview and guidelines. J Bus Res. 2021;133:285-96.
20. Pedersen BK, Febbraio MA. Muscles, exercise and obesity: skeletal muscle as a secretory organ. Nat Rev Endocrinol. 2012;8:457-65.
21. Park KH, Zaichenko L, Brinkoetter M, et al. Circulating irisin in relation to insulin resistance and the metabolic syndrome. J Clin Endocrinol Metab. 2013;98:4899-907.
22. Perakakis N, Triantafyllou GA, Fernandez-Real JM, et al. Physiology and role of irisin in glucose homeostasis. Nat Rev Endocrinol. 2017;13:324-37.
23. Jedrychowski MP, Wrann CD, Paulo JA, et al. Detection and quantitation of circulating human irisin by tandem mass spectrometry. Cell Metab. 2015;22:734-40.
24. Polyzos SA, Anastasilakis AD, Efstathiadou ZA, et al. Irisin in metabolic diseases. Endocrine. 2018;59:260-74.
25. Xiong XQ, Chen D, Sun HJ, et al. FNDC5 overexpression and irisin ameliorate glucose/lipid metabolic derangements and enhance lipolysis in obesity. Biochim Biophys Acta. 2015;1852:1867-75.
26. Khalil RG, Atia T, Yousef AI, et al. Role of irisin in metabolic and cardiovascular disorders and its therapeutic potential. Beni-Suef U J Basic. 2025;14.
27. Zhu D, Zhang X, Wang F, et al. Irisin rescues diabetic cardiac microvascular injury via ERK1/2/Nrf2/HO-1 mediated inhibition of oxidative stress. Diabetes Res Clin Pract. 2022;183:109170.

DOI: 10.5455/medscience.202509.259

28. Chi C, Fu H, Li YH, et al. Exerkine fibronectin type-III domain-containing protein 5/irisin-enriched extracellular vesicles delay vascular ageing by increasing SIRT6 stability. Eur Heart J. 2022;43:4579-95.

29. Wang PW, Pang Q, Zhou T, et al. Irisin alleviates vascular calcification by inhibiting VSMC osteoblastic transformation and mitochondria dysfunction via AMPK/Drp1 signaling pathway in chronic kidney disease. Atherosclerosis. 2022;346:36-45.

30. Wang S, Hu S, Pan Y. The emerging roles of irisin in vascular calcification. Front Endocrinol (Lausanne). 2024;15:1337995.

31. Fu J, Han Y, Wang J, et al. Irisin Lowers Blood Pressure by Improvement of Endothelial Dysfunction via AMPK-Akt-eNOS-NO Pathway in the Spontaneously Hypertensive Rat. J Am Heart Assoc. 2016;5:e003433.

32. Li RL, Zhuo CL, Yan X, et al. Irisin attenuates vascular remodeling in hypertensive mice induced by Ang II by suppressing Ca(2+)-dependent endoplasmic reticulum stress in VSMCs. Int J Biol Sci. 2024;20:680-700.

33. Qin SG, Tian ZJ, Boidin M, et al. Irisin is an Effector Molecule in Exercise Rehabilitation Following Myocardial Infarction (Review). Front Physiol. 2022;13:935772.

34. Lu L, Ma J, Tang J, et al. Irisin attenuates myocardial ischemia/reperfusion-induced cardiac dysfunction by regulating ER-mitochondria interaction through a mitochondrial ubiquitin ligase-dependent mechanism. Clin Transl Med. 2020;10:e166.

35. Aronis KN, Moreno M, Polyzos SA, et al. Circulating irisin levels and coronary heart disease: association with future acute coronary syndrome and major adverse cardiovascular events. Int J Obes (Lond). 2015;39:156-61.

36. Pan JA, Zhang H, Yu Q, et al. Association of Circulating Irisin Levels and the Characteristics and Prognosis of Coronary Artery Disease. Am J Med Sci. 2021;362:63-71.

37. Sun Z, Wu Z, Zhu L, et al. Research trends and hotspot evolution of exercise-regulated myokines: a bibliometric analysis from 2003 to 2023. Front Physiol. 2024;15:1410068.