

Therapeutic and Pathogenic Dimensions of Extracellular Vesicles: A Decade of Comparative Bibliometric Mapping (2014–2024)

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ABSTRACT

Background: Extracellular vesicles (EVs) embody a central paradox in contemporary biomedicine—acting simultaneously as mediators of disease and as vehicles for therapeutic innovation. Despite the exponential growth of literature exploring these dual roles, a comprehensive quantitative comparison of EV research in therapy and pathogenesis has remained unexplored. **Objective:** This study addresses this gap through a systematic bibliometric analysis of global EV research (2014–2024), providing a visual overview of the current research landscape, emerging trends, and the convergence potential between therapeutic and pathogenic domains. **Methods:** Conducted in accordance with the PRISMA framework, this bibliometric investigation utilized the Scopus database. A structured search identified 58,314 publications, with 15,153 (therapy) and 7,776 (pathogenesis) meeting the inclusion criteria. VOSviewer (version 2010) was employed for network construction and visualization of keyword co-occurrence, citation networks, and thematic clusters. **Results:** The analysis uncovered a definitive paradigm shift, with therapeutic output overtaking pathogenesis in 2019 and maintaining a steeper growth trajectory. However, this quantitative transition conceals a deep-seated structural divide. The two domains have evolved as distinct intellectual silos, with specialized high-impact clusters pathogenesis in neurodegenerative biomarkers (FWCI=2.80) and therapy in delivery platforms like mRNA vaccines (FWCI=2.63). Crucially, this segregation is reified by geographically distinct collaborative networks and a parallel, non-interacting investigation of shared biological mechanisms (e.g., neural communication). **Conclusion:** This study provides the first quantitative map of the EV field's dualism, revealing that its central challenge is not a lack of activity, but a lack of integration. The findings underscore an urgent need to forge strategic links between pathogenic insight and therapeutic engineering to unlock the full clinical potential of EVs.

Keywords: Extracellular Vesicles- (EVs), Exosomes, Bibliometric Analysis, EVs Therapeutic Potential, EVs Pathogenic potentiel, Translational Research, Double-Edged Sword

INTRODUCTION

The discovery of extracellular vesicles (EVs), particularly exosomes, as key facilitators of intercellular communication has fundamentally reshaped our understanding of human physiology and disease pathogenesis. Once dismissed as cellular debris, these nanoscale lipid bilayers are now recognized as sophisticated carriers of a complex molecular cargo, capable of reprogramming recipient cell functions across biological systems [1-3]. This pivotal role, however, is characterized by a profound and consequential duality, presenting a central paradox in modern biomedicine [4]. On one front EVs are hailed as a revolutionary therapeutic platform. Their innate biocompatibility, low immunogenicity, and exceptional ability to traverse biological barriers have positioned them as ideal candidates for next-generation drug delivery systems, regenerative medicine, and vaccines [5]. The scientific narrative in this domain is one of immense promise, exploring engineered exosomes as targeted missiles against cancer and native vesicles as restorative agents in tissue repair. Concurrently, a parallel and equally vigorous body of literature casts EVs in a more sinister light. The very mechanisms that underpin their therapeutic potential are the same properties that enable them to act as pathogenic vectors. In cancer, they prepare the metastatic niche [6, 7]; in neurodegenerative disorders, they propagate misfolded proteins [8]; and in chronic inflammatory diseases [9], they amplify destructive

immune responses [10]. This dichotomy frames EVs as a true "double-edged sword" in human health. Over the past decade, research exploring these opposing narratives has expanded at an exponential rate, generating a vast, fragmented, and increasingly complex corpus of literature [11]. While numerous qualitative reviews have synthesized the biological mechanisms or clinical potential within each silo therapy or pathogenesis [12-14] a critical gap remains. The scientific community lacks a comprehensive, quantitative synthesis that maps the intellectual structure and evolutionary trajectories of these two domains in relation to one another. Key questions persist: How do the scale, growth, and collaborative networks of the "therapeutic" paradigm compare to those of the "pathogenic" paradigm? Where are the intellectual crossroads, and where do conceptual chasms exist? What are the emergent research fronts that may represent the convergence of these two paths. To address this gap, we present a systematic bibliometric analysis of the scientific literature on exosomes and extracellular vesicles from 2014 to 2024. This study is grounded in a systematic literature search and selection process, designed to comprehensively capture and contrast the 'therapeutic' and 'pathogenic' research domains of EVs. By employing established bibliometric techniques including co-word, citation network, and burst analysis—we aim to:

- Quantify and contrast the developmental trajectories and research volume dedicated to EV-based therapy versus pathogenesis.
- Delineate the intellectual architecture of each domain, identifying foundational papers, key thematic clusters, and influential contributors.
- Uncover emerging trends and forecast potential future research directions, particularly at the interface where therapeutic innovation seeks to counteract pathogenic mechanisms.

Therefore, the objective of this bibliometric evaluation was to provide responses to the following research inquiries :

- What are the annual publication trends on the therapeutic and pathogenic roles of extracellular vesicles from 2014 to 2024?
- Which countries have the highest scientific output on extracellular vesicles in both therapeutic and pathogenic research domains?
- Which institutions have the highest scientific output on extracellular vesicle research in both therapeutic and pathogenic domains?

- Who are the leading authors in extracellular vesicle (EV) research across therapeutic and pathogenic domains?

- What are the high-impact research topics (according Field-Weighted Citation Impact :FWCI) in therapeutic versus pathogenic extracellular vesicle domains?

- Which keywords most prominently characterize the therapeutic and pathogenic research domains of extracellular vesicles based on bibliometric mapping?

- Which journals are the leading sources of publications on extracellular vesicle research in both therapeutic and pathogenic domains?

- What are the most highly cited publications in extracellular vesicle research for therapeutic and pathogenic domains between 2014 and 2024?

This systematic mapping is intended to provide an evidence-based framework for the scientific community, offering invaluable insights for navigating the current landscape and strategically guiding future inquiry.

Method

Research Design

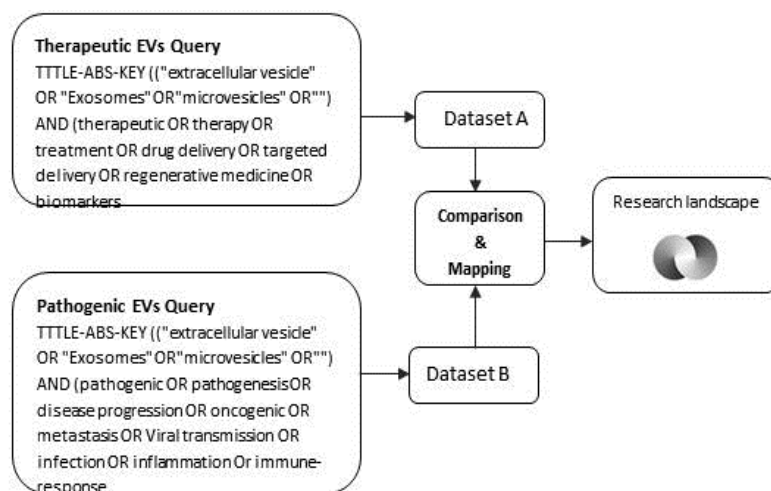


FIGURE 1: Research Design and Workflow for Comparative Bibliometric Analysis of Extracellular Vesicles between both Sides (Therapeutic and Pathogenic)

This bibliometric analysis was designed to explore the scientific landscape of extracellular vesicle (EV) research by examining both their therapeutic and pathogenic dimensions (Figure 1). To achieve this, two distinct datasets were constructed:

- Dataset A (Therapeutic EVs Query): Focused on the therapeutic side of extracellular vesicles (EVs), encompassing studies investigating their potential roles in treatment development and clinical translation, incorporating keywords related to *therapy*, *treatment*, *drug delivery*, *regenerative medicine*, and *diagnostics*.
- Dataset B (Pathogenic EVs Query): Targeted studies exploring disease-associated or detrimental roles of EVs, using terms such as *pathogenesis*, *biomarkers*, *disease progression*, *oncogenesis*, *infection*, and *inflammation*.

Both datasets were retrieved from Scopus using advanced searches of titles, abstracts, and keywords. They were analyzed independently

and comparatively to identify overlaps, emerging trends, and dominant themes within extracellular vesicle (EV) research. Following the PRISMA framework [15], the study systematically mapped leading countries, institutions, journals, authors, and keywords in the therapeutic (Dataset A) and pathogenic (Dataset B) domains. Bibliometric visualization was performed using VOSviewer, enabling the construction of co-authorship, citation, and keyword networks that revealed key research linkages and evolving trends across the global EV landscape.

Identification

Data Base Selection

This review was conducted on september 7th, 2025. The Scopus database was selected as the primary source of data, given its recognized reliability and broad coverage of peer-reviewed scientific literature. Scopus was also chosen as it represented the only accessible database for this analysis.

Search Strings

To ensure accurate retrieval of relevant studies, the search strategy for Dataset (A) representing the therapeutic side of extracellular vesicles (EVs) employed a set of precisely defined keywords specific to this research domain. The keywords used for Dataset A (therapeutic side of exosomes) were as follows:)

"extracellular vesicles OR exosome OR microvesicles AND therapeutic OR therapy OR treatment OR regenerative", for instance TITLE-ABS-KEY (extracellular vesicles OR exosome OR exosomes OR microvesicles AND therapeutic OR therapy OR treatment OR regenerative OR drug delivery OR Biomarker OR gene delivery). Moreover, publication for the last decade were selected from 2014 to 2024, for instance " AND PUBYEAR > 2013 AND PUBYEAR < 2025 AND PUBYEAR > 2013 AND PUBYEAR < 202 5 AND". In addition, subject area was limited to biochemistry , genetics and molecular biology ; medicine; chemistry ;Immunoloy and microbiology ; chemical engineering ; neuroscience ; engineering ; pharmacology , toxicology and pharmaceutics ; agricultural and biological sciences, for instance (LIMIT-TO (SUBJAREA , "BIOC") OR LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "PHAR") OR LIMIT-TO (SUBJAREA , "ENGI") OR LIMIT-TO (SUBJAREA , "CENG") OR LIMIT-TO (SUBJAREA , "IMMU") OR LIMIT-TO (SUBJAREA , "NEUR") OR LIMIT-TO (SUBJAREA , "AGRI"). Publication in English were selected in this review, for instance AND (LIMIT-TO (LANGUAGE, "English")). to be more accurate exact key words for example: EXACTKEYWORD , ""Exosomes") OR LIMIT-TO (EXACTKEYWORD , "Exosome") OR LIMIT-TO (EXACTKEYWORD , "Extracellular Vesicles") OR LIMIT-TO (EXACTKEYWORD , "Tissue Regeneration") OR LIMIT-TO (EXACTKEYWORD , "Therapy Effect") OR LIMIT-TO (EXACTKEYWORD , "Animal Experiment") OR LIMIT-TO (EXACTKEYWORD , "Human") OR LIMIT-TO (EXACTKEYWORD , "Humans") OR LIMIT-TO (EXACTKEYWORD , "Drug Delivery") OR LIMIT-TO (EXACTKEYWORD , "Regenerative ") OR LIMIT-TO (EXACTKEYWORD , "Biomarkers") OR LIMIT-TO (EXACTKEYWORD , "Regenerative Medicine"). Publication were limited to articles only AND (LIMIT-TO (DOCTYPE, "ar")). Finally, journals were the only source in this review AND (LIMIT-TO (SRCTYPE, "j")).

Inclusion and Exclusion Criteria

Screening and Selection

Table 1: Inclusion and Exclusion Criteria

Dataset A		Dataset B	
Inclusion Criteria	Exclusions	Inclusion	Exclusion
Extracellular Vesicles or Exosomes and Therapeutic or Therapy or Treatment	pathogenesis" OR " pathogenic" OR " tumorigenesis or carcinogenesis	Extracellular vesicles Or Exosomes and pathogenesis or pathogenic or pathogenicity	therapy, treatment, therapeutic, drug delivery, delivery, protective and facilitate and regenerative and healing and suppresses facilitate and protocol
2014-2024	All publication before 2014 were excluded and 2025 publications were excluded	2014-2024	All publication before 2014 were excluded and 2025 publications were excluded
English Languages	Any other language	English languages	Any other language
Articles	Thesis, books, conferences, books chapters, blogs	Articles	Thesis, books, conferences, books chapters, blogs
Journals	Any other sources were excluded	Journals	Any other sources were excluded

For Section A, the main keywords used were “*extracellular vesicles*” and “*therapeutic*.” The initial search retrieved 41,068 documents. After applying the inclusion and exclusion criteria (as detailed in Table 01), the number of eligible publications was reduced to 15,153, with 25,915 records excluded.

For Section B, the main keywords used were “*extracellular vesicles*” and “*pathogenic*.” The initial search yielded 12,246

Similarly, for Dataset B, which encompasses the pathogenic side of extracellular vesicles, specific search terms were selected to identify studies addressing disease mechanisms, biomarkers, and pathological processes. The keywords used for Dataset B (pathogenic side of exosomes) were as follows:

"extracellular vesicles OR exosome OR microvesicles AND pathogenesis or pathogenic or for instanceTITLE-ABS KEY ("cancer" OR "carcinoma" OR "metastasis" OR "metastatic" OR "progenitor"

OR "melanoma" OR "melanomaexosomes" OR "premetastatic" OR "parkinson" OR "Alzheimer" OR "fibrosis" OR "inflammation" OR "neurodegenerative" OR "mediators" OR "tumorigenesis" OR "oncogenic" OR "immune evasion" OR "viral transmission" OR "pathogenesis " OR "kidney diseases " OR "disease progression" OR "infection").

Additionally, certain keywords were excluded to prevent overlap with the therapeutic dataset and ensure the specificity of the pathogenic search strategy, for instance , AND NOT TITLE-ABS-KEY ("therapy" OR "treatment" OR "therapeutic" OR "drug delivery" OR "delivery" OR "protective" OR "facilitate" OR "regenerative" OR "healing" OR "glymphatic" OR "suppresses" OR "facilitate" OR "protocol")).Moreover , publication for the last decade were selected from 2014 to 2024, for instance " AND PUBYEAR > 2013 AND PUBYEAR < 2025 AND PUBYEAR > 2013 AND PUBYEAR < 202 5 AND". In addition, subject area was limited to biochemistry, genetics and molecular biology; medicine; chemistry; Immunoloy and microbiology; chemical engineering; neuroscience; engineering; pharmacology, toxicology and pharmaceutics; agricultural and biological sciences. For instance, (LIMIT-TO (SUBJAREA, "BIOC") OR LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "CHEM") OR LIMIT-TO (SUBJAREA , "IMMU") OR LIMIT-TO (SUBJAREA , "CENG") OR LIMIT-TO (SUBJAREA , "NEUR") OR LIMIT-TO (SUBJAREA , "PHAR") OR LIMIT-TO (SUBJAREA , "ENGI") OR LIMIT-TO (SUBJAREA , "AGRI")) Publication were limited to articles only AND (LIMIT-TO (DOCTYPE, "ar")). Finally, journals were the only source in this review AND (LIMIT-TO (SRCTYPE, "j")).

documents, which, after applying the same criteria (Table 01), were reduced to 7,776 publications, following the exclusion of 4,470 records.

Inclusion and Reporting

The findings of this bibliometric analysis are presented according to the PRISMA framework (Figure 02) [15].

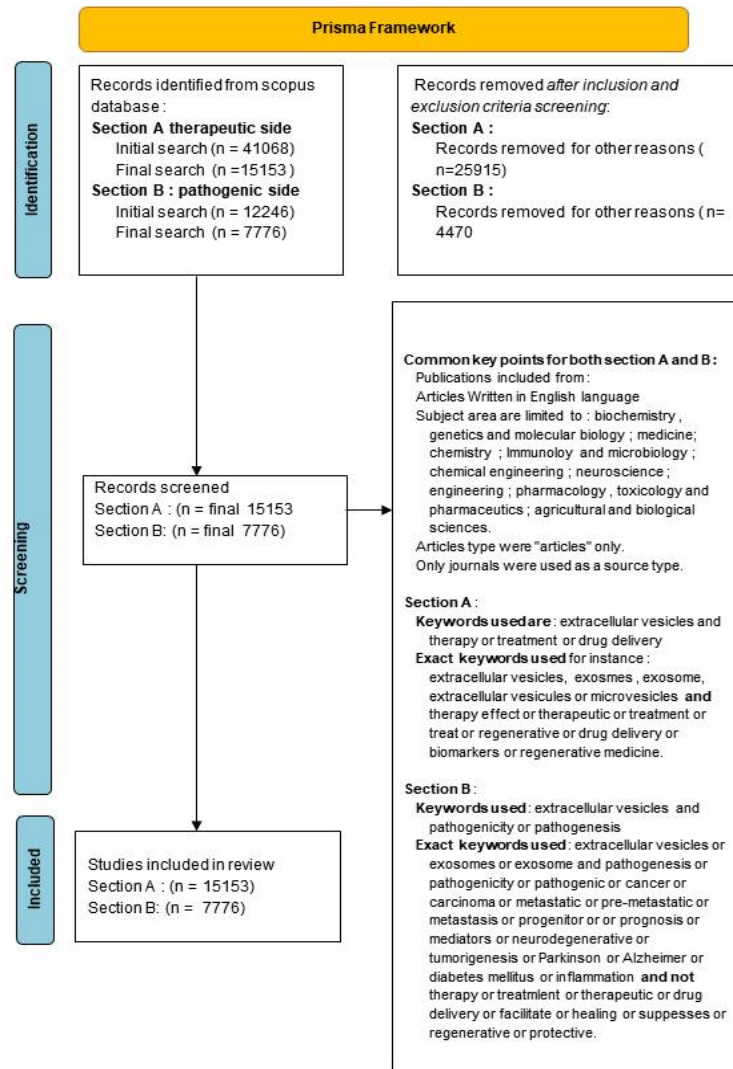


FIGURE 2: PRISMA Flow Diagram of the Bibliometric Selection Process for Extracellular Vesicle Research in Therapeutic and Pathogenic Contexts

Results

In this section, we address the research questions formulated for this bibliometric analysis

What are the annual publication trends on the therapeutic and pathogenic roles of extracellular vesicles from 2014 to 2024?

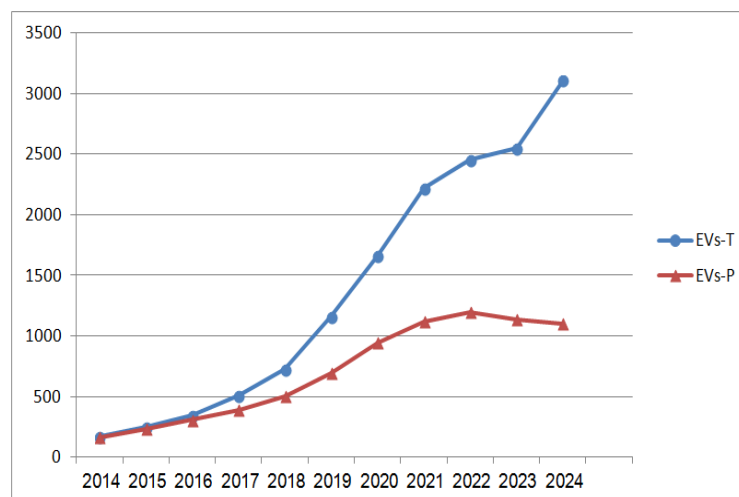


FIGURE 3: Comparative Publication Output in the Pathogenic and Therapeutic Domains of Extracellular Vesicle Research over the Decade 2014–2024.

EVs-T: Studies About Therapeutic Side of Extracellular Vesicles, EVs-P: Studies About Pathogenic Side of Extracellular Vesicles

Figure 3 illustrates the steady rise of extracellular vesicle (EV) research from 2014 to 2024, highlighting distinct trends between therapeutic (EVs-T) and pathogenic (EVs-P) studies. Early in the decade, pathogenic research dominated; however, between 2020 and 2021, therapeutic studies gained momentum and soon surpassed pathogenic ones. Since then, EVs-T has shown a sharper growth curve,

reflecting increasing scientific and clinical focus on therapeutic applications, while EVs-P output has continued to rise more moderately.

Which countries have the highest scientific output on extracellular vesicles in both therapeutic and pathogenic research domains?

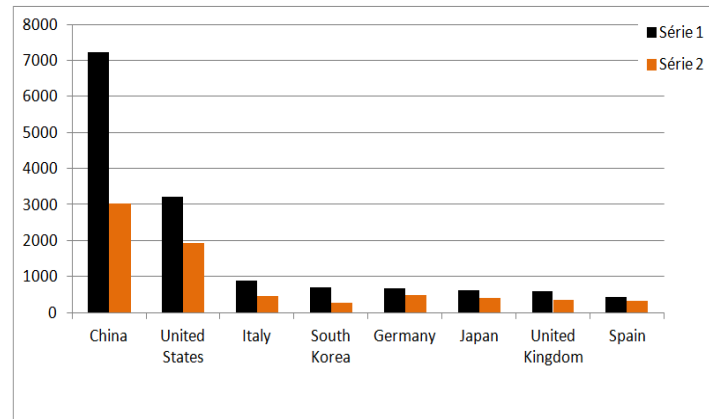


Figure 4: A Comparative Analysis of the Top Eight Contributing Countries to Extracellular Vesicles Research Both in Therapeutic Applications (EVs-T) vs. Pathogenic Roles (EVs-P) (2014–2024).

EVs-T: studies About Therapeutic Side of Extracellular Vesicles, Evs-P: Studies About Pathogenic Side of Extracellular Vesicles

Figure 4 illustrates the scientific output of the top eight countries in extracellular vesicle (EV) research (2014–2024). China and the United States lead the field, with China showing a strong emphasis on the therapeutic domain (EVs-T; ratio = 2.38), while the U.S. displays a more balanced profile across both therapeutic and pathogenic areas. After these two frontrunners, publication output declines notably. Italy

ranked as Europe's top contributor, maintaining balanced productivity between both domains (ratio = 1.92). South Korea, Germany, Japan, the United Kingdom, and Spain follow with comparable outputs, all showing a moderate preference toward therapeutic EV research. Which institutions have the highest scientific output on extracellular vesicle research in both therapeutic and pathogenic domains?

Table 2: Top Seven Leading Institutions in Extracellular Vesicle Research Across Therapeutic and Pathogenic Domains, Based on the Highest Number of Publications

EVs and Therapeutic Domain				EVs and Pathogenic Domains			
Rank	Country	TP	Most significant academic institutions	Country	TP	Most significant academic institutions	
1	China	7223	CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, National Center for Nanoscience and Technology of China, Beijing 100190, China	China	3034	Department of Pathology, Nanfang Hospital, Southern Medical University, Guangzhou, 510515, Guangdong Province, China	
2	United State	3221	Center for Nanotechnology in Drug Delivery, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States	United State	1928	Children's Cancer and Blood Foundation Laboratories, Departments of Pediatrics, Weill Cornell Medical College, New York, 10021, NY, United States	
3	Italy	885	Department of Veterinary Medicine, University of Perugia, Italy	Germany	476	German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany	
4	South Korea	709	Department of Bio and Brain Engineering, KAIST, Daejeon, 34141, South Korea	Italy	461	Department of Oncology and Molecular Medicine, Istituto Superiore di Sanità, Viale Regina Elena 299, Rome, 00161, Italy	
5	Germany	663	Institute of Molecular and Translational Therapeutic Strategies, Integrated Research and Treatment Center Transplantation (IFB-Tx), Hannover Medical School, 30625 Hannover, Carl-Neuberg-Str. 1, Germany	Japan	405	Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Tokyo 104-0045, Japan	
6	Japan	617	Department of Frontier Science for Cancer and Chemotherapy, Osaka University, Graduate School of Medicine, Chuo-ku Tokyo, Suita, 565-0871, Osaka, Japan	UK	363	Section of Oncology, School of Medicine, Cardiff University, Cardiff, CF14 2TL, United Kingdom	
7	United King-Dom	582	MRC London Institute of Medical Sciences (LMS), London, W12 0NN, United Kingdom	Spain	323	Fundación de Investigación HM Hospitales, HM Hospitales, Madrid, Spain	

TP: Total Publication

The distribution of scientific output across the most prolific institutions is detailed in Table 2, further refining the geographic trends observed in Figure 2.

In the therapeutic domain (EVs-T), the CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety (China) led

global output with 7,223 publications, followed by the University of North Carolina at Chapel Hill's Center for Nanotechnology in Drug Delivery (USA, 3,221).

In Europe, the University of Perugia (Italy, 885) was the most active contributor. Conversely, in the pathogenic domain (EVs-P), the

Department of Pathology at Nanfang Hospital, Southern Medical University (China) ranked first with 8,034 publications, ahead of the Children's Cancer and Blood Foundation Laboratories at Weill Cornell Medical College (USA, 1,928). The German Center for

Neurodegenerative Diseases (DZNE) emerged as Europe's leading institution in pathogenic EV research.

Who are the leading authors in extracellular vesicle (EV) research across therapeutic and pathogenic domains?

Table 3: Top 07 Authors for both Section (A and B) (year from 2014 –to 2024) with Top Topic of Research in Both Fields

EVs and Therapeutic Domain					EVs and Pathogenic Domains				
Author	TP	h-index	TC	Current affiliation	Author	TP	TC	h-index	Current affiliation
Camussi, Giovanni	35618	96	51137	Università degli Studi di Torino, Scuola di MedicinaThe institution will open in a new tab, Turin, Italy	Kapogiannis, Dimitrios	201	12720	60	National Institute on Aging (NIA)The institution will open in a new tab, Bethesda, United state
Xu, Wenrong	303	75	20816	AoYoung HospitalThe institution will open in a new tab, Zhangjiagang, China	Peinado, Héctor	121	40581	54	Centro Nacional de Investigaciones OncológicasThe institution will open in a new tab, Spain
Giebel, Bernd	176	53	28517	Universitätsklinikum EssenThe institution will open in a new tab, Essen, Germany	MacKman, Nigel	551	47878	116	UNC School of MedicineThe institution will open in a new tab, Chapel Hill, United state
Chopp, Michael	836	142	75443	Henry Ford HospitalThe institution will open in a new tab, Detroit, United state	Zhu, W	138	6329	47	Jingjiang People's HospitalThe institution will open in a new tab, Jingjiang, china
Ochiya, Takahiro	212	43	7675	The Japanese Society for Regenerative Medicine, Tokyo, Japn	Goetzl, E.J	482	31269	101	UCSF School of MedicineThe institution will open in a new tab, San Francisco, United state
Vader, Pieter	102	48	25961	University Medical Center UtrechtThe institution will open in a new tab, Utrecht	Kim, Y.K	229	16135	60	MD Healthcare Inc.The institution will open in a new tab, Seoul, South korea
Wang, Yang	130	43	7840	Shanghai Sixth People's HospitalThe institution will open in a new tab,shanghai, china	Nieuwlan, R	296	34462	79	Universiteit van AmsterdamThe institution will open in a new tab, Amsterdam. Netherlands

TC: Total of Citation, TP: Total of Publication

Table 3 presents the leading authors in EV research. In the therapeutic domain, *Giovanni Camussi* (Italy) shows the highest citation impact (h-index 96; TC 51,137), while *Michael Chopp* (USA) stands out for productivity (TP 836; TC 75,443). In the pathogenic domain, *Nigel Mackman* (USA; TP 551) and *Dimitrios Kapogiannis* (USA) lead key studies on coagulation and neurodegeneration. The

inclusion of authors from China and Spain underscores the global reach of EV research.

What are the high-impact research topics by field-weighted citation impact (FWCI) in therapeutic versus pathogenic extracellular vesicle domains?

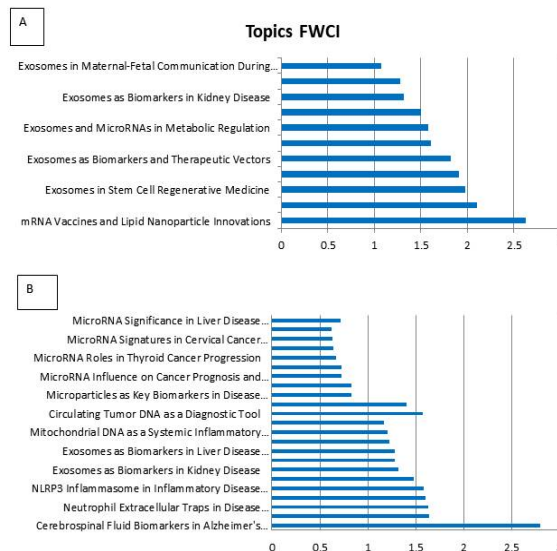


Figure 5: Top Research Topics of Research by Field-Weighted Citation Impact (FWCI) for the (A) Therapeutic Applications and (B) Pathogenic Roles of Extracellular Vesicles (EVs).

The Field-Weighted Citation Impact (FWCI) provides a bibliometric indicator of the most influential research themes in extracellular vesicle (EV) studies across both therapeutic and pathogenic domains (Figure 5).

In the pathogenic domain, high-impact topics cluster around neurodegeneration, cancer genomics, and inflammation. The leading theme, “Cerebrospinal Fluid Biomarkers in Alzheimer’s Disease” (FWCI = 2.80), reflects the prominence of EVs in neurodegenerative diagnostics. Oncology-related topics such as “Circulating Tumor DNA as a Diagnostic Tool” (FWCI = 1.57) and “CircRNAs in Cancer Progression” (FWCI = 1.40) further emphasize their role in tumor biology, while mechanisms like “Neutrophil Extracellular Traps” and the “NLRP3 Inflammasome” (FWCI $\approx$ 1.6) highlight EV-mediated

immune modulation in disease. In the therapeutic domain, research impact is concentrated in drug delivery and regenerative applications.

The top-ranked topic, “mRNA Vaccines and Lipid Nanoparticle Innovations” (FWCI = 2.63), showcases the growing integration of EVs with nanomedicine. Complementary themes include “Exosomes in Stem Cell Regenerative Medicine” (FWCI = 1.98) and “Nanoparticle Strategies for Blood–Brain Barrier Delivery” (FWCI = 1.61), underscoring the field’s translational momentum toward clinical application.

Which keywords most prominently characterize the therapeutic and pathogenic research domains of extracellular vesicles based on bibliometric mapping?

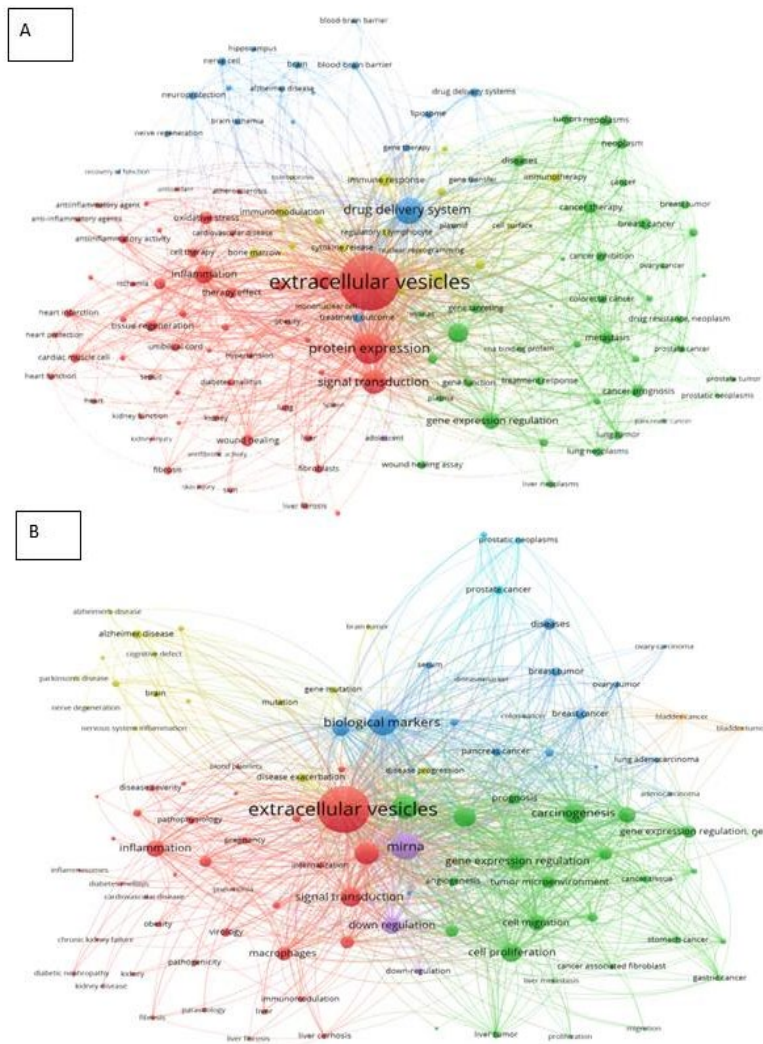


Figure 6: VOSviewer Network Mapping of Research Keywords in Extracellular Vesicle Studies: (A) Therapeutic Domain and (B) Pathogenic Domain.

Figure 6 illustrates the keyword co-occurrence networks in extracellular vesicle research, highlighting clear thematic distinctions between therapeutic and pathogenic studies. In the therapeutic network, clusters centered on translational and regenerative themes, linking “extracellular vesicles” with “drug delivery systems,” “nanovesicles,” and the “blood–brain barrier.” Related clusters emphasized “wound healing,” “tissue regeneration,” and “immune modulation,” reflecting the growing focus on clinical and bioengineering applications. In contrast, the pathogenic network was organized around mechanistic and diagnostic themes. Central clusters

connected “extracellular vesicles” to “biological markers” and “signal transduction,” extending to disease-related terms such as “carcinogenesis,” “cell proliferation,” and “gene regulation.” The limited overlap between both maps underscores the conceptual divide in how EVs are studied as therapeutic tools versus mediators of pathology.

Which journals are the leading sources of publications on extracellular vesicle research in both therapeutic and pathogenic domains?

Table 4 : Top Seven Journals in Extracellular Vesicle Research: Therapeutic (Section A) vs. Pathogenic Domains, according to the Number of Publications Indexed in the Scopus Database

EVs and Therapeutic Domain						EVs and Pathogenic Domains				
	Journal	TP	TC	Cite Score	Publisher	Journal	TP	TC	Cite Score	Publisher
1	International Journal of Molecular Sciences	59908	537397	9.0	MDPI	International Journal of Molecular Sciences	59908	537397	9.0	MDPI
2	Stem Cells Research and Therapy	1888	25054	13.3	Springer nature	Journal of extracellular vesicles	435	11281	25.9	John wiley and sons
3	Journal of Extracellular Vesicles	435	11281	25.9	John wiley and sons	Frontiers in immunology	12444	37067	16.8	Frontier media S.A
4	Journal of Nanobio-Technology	1888	25054	13.3	Springer nature	cancers	22133	194180	8.8	MDPI
5	Cells	122444	131259	10.5	MDPI	analytical chemistry	8482	98484	11.6	American chemical society
6	Frontiers in Immunology	12444	37067	16.8	Frontier media S.A	oncotarget	449	2495	5.6	Impact journals
7	Theranostics	1686	40343	23.9	vyspring International Publisher	cells	12444	131259	10.5	(MDPI)

TP: Total Publication, TC: Total Citation, MDPI: Multi-Disciplinary Digital Publishing Institute

The analysis of publication patterns revealed the journals most active in disseminating research on the therapeutic and pathogenic roles of extracellular vesicles (Table 4). In the therapeutic domain, *International Journal of Molecular Sciences* (MDPI) led in publication volume (TP = 59,908; TC = 537,397), followed by *Cells* (MDPI, TP = 122,444) and *Stem Cell Research & Therapy* (Springer Nature, TP = 1,888). High-impact titles such as *Journal of Extracellular Vesicles* (CiteScore = 25.9) and *Theranostics* (CiteScore = 23.9) reflected the field's translational and clinical focus. In the pathogenic domain, *International Journal of*

Molecular Sciences again ranked first, but the publication landscape shifted toward disease-oriented journals, notably *Cancers* (MDPI, TP = 22,133), *Frontiers in Immunology* (TP = 12,444), and *Nature Communications* (Springer Nature, TP = 32,699; TC = 764,101). Here too, the *Journal of Extracellular Vesicles* remained the top-cited and highest-impact platform (CiteScore = 25.9).

What are the most highly cited publications in extracellular vesicle research for therapeutic and pathogenic domains between 2014 and 2024?

Table 5(a): Top Five Most Cited Publications in Extracellular Vesicle Research: Therapeutic vs. Pathogenic Domains (2014-2024)

EVs and Therapeutic Domain					EVs and Pathogenic Domains				
Article Title	Authors	Year of Publication	Citation	Journal	Article title	authors	Year of Publication	Citation	Journal
Exosomes as Drug Delivery Vehicles for Parkinson's Disease Therapy	Haney, M.J., Klyachko, N.L., Zhao, Y., ... Kabanov, A.V., Batrakova, E.V. [16]	2015	1681	Journal of controlled release	Pancreatic cancer exosomes initiate pre-metastatic niche formation in the liver	Costa-saliva et al. [17]	2015	2022	Nature cell biology
Minimal Information for Studies of Extracellular Vesicles (MISEV2023): From Basic to Advanced Approaches	Welsh, J.A., Goberdhan, D.C.I., O'Driscoll, L., ... Zubair, H. [18]	2024	1557	Journal of extracellular vesicles	Cancer-Secreted miR-105 destroys vascular endothelial barriers to promote metastasis	Zhou et al. [19]	2014	1267	Cancer cell
A Doxorubicin Delivery Platform Using Engineered Natural Membrane Vesicle Exosomes for Targeted Tumor Therapy	Tian, Y., Li, S., Song, J., ... Wei, J., Nie, G. [20]	2014	1554	biomaterials	Extracellular Vesicle and Particle Biomarkers Define Multiple Human Cancers	Hoshino et al. [21]	2020	897	cell

Table 5(b): Top Five Most Cited Publications in Extracellular Vesicle Research: Therapeutic vs. Pathogenic Domains (2014–2024)

EVs and Therapeutic Domain					EVs and Pathogenic Domains				
Article Title	Authors	Year of Publication	Citation	Journal	Article title	authors	Year of Publication	Citation	Journal
Development of Exosome-Encapsulated Paclitaxel to Overcome MDR in Cancer Cells	Kim, M.S., Haney, M.J., Zhao, Y., ... Kabanov, A.V., Batrakova, E.V. [22]	2016	1277	Nanomedicine nanotechnology biology and medicine	Identification of doublestranded genomic dna spanning all chromosomes with mutated KRAS and P53 DNA in the serum exosomes of patients with pancreatic cancer	kahlert	2014	867	Journal of biological chemistry
Depletion of Microglia and Inhibition of Exosome Synthesis Halt Tau Propagation	Asai et al. [23]	2015	1257	Nature neurosciences	Tumor microenvironment derived exosomes pleiotropically modulate cancer cell metabolism	Zhao et al. [24]	2016	782	Elife

Analysis of citation patterns revealed the most influential publications in extracellular vesicle (EV) research across both therapeutic and pathogenic domains between 2014 and 2024 (Table 05). In the therapeutic domain, the most cited study was by Haney et al. [16], “Exosomes as drug delivery vehicles for Parkinson’s disease therapy,” published in the *Journal of Controlled Release* (1,681 citations). It was followed by the MISEV2023 guidelines (Welsh et al. [18]; *Journal of Extracellular Vesicles*, 1,557 citations) and Tian et al. [20] on doxorubicin delivery using engineered exosomes in *Biomaterials* (1,554 citations). Collectively, these studies highlight the field’s emphasis on exosome engineering and targeted drug delivery. In the pathogenic domain, the most cited work was Costa-Silva et al. [17], “Pancreatic cancer exosomes initiate pre-metastatic niche formation in the liver,” published in *Nature Cell Biology* (2,022 citations). It was followed by Zhou et al. [19] in *Cancer Cell*, which examined exosomal miR-105 in metastasis (1,267 citations), and Hoshino et al. [21] in *Cell*, defining EV biomarkers across multiple cancers (887 citations). Together, these landmark studies underscore the pivotal role of EVs in cancer progression, intercellular communication, and biomarker discovery.

Discussion

This bibliometric analysis aims to provide a quantitative foundation for understanding how the scientific community has approached the paradoxical nature of extracellular vesicles over the past decade. Our systematic investigation reveals a field defined by a fundamental dichotomy: while foundational research on pathogenic mechanisms initially dominated, a significant evolutionary trajectory has now established a dominant focus on therapeutic applications. However, these two paradigms remain intellectually and geographically distinct, representing parallel yet segregated paths of inquiry. This discussion will explore this central tension by interpreting three interconnected trends derived from our analysis of publication patterns, research themes, and collaborative networks:

- the precise evolutionary trajectory from pathogenesis to therapy;
- the persistent intellectual and collaborative segregation between these domains; and
- the emergence of translational bridge themes, such as 'drug delivery' and 'engineering,' which signal the field's nascent efforts to integrate mechanistic understanding with clinical innovation.

Unpacking these trends is critical, as this central tension—between understanding EV-driven disease and harnessing EV-based cures—defines the current landscape and outlines the fundamental challenge of safely translating EV potential into clinical applications..

Trends in Publication

The evolution of publication output between 2014 and 2024 clearly illustrates a shifting scientific narrative surrounding extracellular vesicles (EVs). During the early years (2014–2017), research on both therapeutic and pathogenic roles progressed at a comparable and modest pace, reflecting the field’s exploratory phase in establishing fundamental biological principles [3]. However, starting in 2018, publications related to the therapeutic applications of EVs began to rise sharply, showing exponential growth and reaching their highest level in 2024. This surge aligns with expanding interest in EVs as nanocarriers for drug delivery and regenerative medicine, a paradigm powerfully articulated in foundational reviews [11], and underscored by growing clinical exploration [5]. In contrast, publications focusing on the pathogenic implications of EVs increased more moderately and peaked around 2019–2022 before slightly declining or plateauing. This period of heightened activity in pathogenesis research may be partially explained by the COVID-19 pandemic, during which EVs were intensively investigated for their roles in viral transmission, inflammation, and immune response [25, 26] (Thery et al., 2009). The growing divergence between the two curves after 2019 highlights a strategic research transition: EVs are increasingly viewed as clinical tools rather than solely as mediators of disease, a shift reflecting the field’s maturation from mechanistic discovery to translational application. Overall, the dominance of therapeutic-focused literature in recent years underscores a concerted effort to harness the dual nature of EVs, moving beyond their characterization as biological risk factors to actively engineer them into biomedical opportunities.

Geographical Distribution and Institutional Hubs in EV Therapeutics and Pathogenesis

The global distribution of extracellular vesicle (EV) research reveals marked disparities in national contributions across therapeutic and pathogenic domains. China and the United States dominate the field, reflecting their strong institutional infrastructure and strategic investment in biomedical innovation. China leads both domains, driven by state-supported initiatives in nanomedicine and regenerative

therapy, exemplified by the CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety. The United States follows with a more diversified ecosystem, where institutions such as the University of North Carolina and Weill Cornell Medical College balance translational and mechanistic studies.

In Europe, Italy and Germany are major contributors—Italy through integrative biomedical research at the University of Perugia, and Germany via disease-focused work at the German Center for Neurodegenerative Diseases (DZNE). Meanwhile, South Korea and Japan are emerging leaders in therapeutic EV engineering, with institutions like KAIST and Osaka University at the forefront of nanotechnological innovation.

Insights from Top Authors, Research Topics, and Keywords on Extracellular Vesicles in Therapy and Pathogenicity

The therapeutic landscape is configured around a translational lexicon, where the central node of "extracellular vesicles" is tightly linked to applied, interventionist terms like "drug delivery system," "wound healing," and "immune modulation." This network structure underscores the field's momentum in harnessing EVs as biological vectors and regenerative mediators. The presence of clusters around "gene therapy," "nanovesicles," and the "blood–brain barrier" visually illustrates the successful integration of bioengineering principles into EV research, bridging fundamental biology with clinical innovation. Gene tarregttingt also talk about key words en commun Conversely, the pathogenicity-oriented keyword map displays a mechanistic and diagnostic emphasis. Here, EVs are positioned at the intersection of "signal transduction," "gene expression regulation," and pathophysiological states like "inflammation," "fibrosis," and "carcinogenesis." The dense clustering of terms such as "tumor microenvironment," "cell proliferation," and "biological markers" highlights the central role of EVs in disease progression and their utility as diagnostic tools. Signal transduction in common This conceptual divide, revealed by the keywords, is powerfully reinforced by the Field-Weighted Citation Impact (FWCI) analysis, which identifies the specific research fronts that are most influential within each paradigm. The pathogenic domain's intellectual pinnacle is occupied by the challenge of neurodegeneration, with the topic "Cerebrospinal Fluid Biomarkers in Alzheimer's Disease" (FWCI 2.80) standing as the single most influential niche. This focus is complemented by high-impact topics in cancer pathogenesis, such as "Circulating Tumor DNA as a Diagnostic Tool" (FWCI 1.57), aligning perfectly with the keyword clusters for "biological markers" and "carcinogenesis." The high impact of this work underscores a research community that rewards the deep, mechanistic dissection of disease [4]. In stark contrast, the therapeutic domain's impact frontier is dominated by delivery engineering and regenerative biology. The highest-impact topic, "mRNA Vaccines and Lipid Nanoparticle Innovations" (FWCI 2.63), perfectly encapsulates the "drug delivery system" and "nanovesicle" keywords, demonstrating a direct synergy between conceptual focus and scholarly impact [27]. Crucially, these distinct intellectual fronts are personified by separate, specialized research communities, creating a social architecture that mirrors the conceptual one. The authors analysis reveals the key actors who embody these paradigms:

The high-impact pathogenic focus on neurodegeneration is championed by Dimitrios Kapogiannis at the National Institute on Aging, whose work on neural-derived exosomes directly

operationalizes the keyword "biological markers" and the high-FWCI topic of Alzheimer's diagnostics. The cancer pathogenesis front, reflected in the keyword cluster for "carcinogenesis," is advanced by leaders like Héctor Peinado (CNIO, Spain), whose seminal work on exosomes in metastasis provides the mechanistic underpinnings for this entire research avenue.

On the therapeutic side, the paradigm of regenerative medicine—evident in the "wound healing" and "tissue regeneration" keywords—is powerfully represented by Giovanni Camussi (University of Turin) and Michael Chopp (Henry Ford Hospital). Similarly, the work of Pieter Vader (UMC Utrecht) embodies the "drug delivery system" keyword, focusing on engineering EVs for nucleic acid delivery, which aligns with the high-impact topic of mRNA vaccine innovations. The overlap of certain keywords, such as "inflammation" and "signal transduction," between the two maps is particularly revealing. It highlights a shared mechanistic foundation where the same molecular pathways can drive both tissue repair and disease progression [10, 17, 28–31]. This conceptual symmetry underscores the pivotal position of EVs as a unifying biological system. However, the fact that these shared mechanisms are investigated by largely distinct author communities (e.g., Kapogiannis in neurodegeneration vs. Camussi in regeneration) indicates a significant opportunity for greater cross-paradigm collaboration. This triangulated bibliometric analysis demonstrates that the "double-edged sword" of extracellular vesicle biology is more than a metaphor; it is the fundamental structural reality of the field's organization. We have delineated two largely distinct, internally cohesive research enterprises one dedicated to deconstructing pathology and the other to constructing therapies each with its own conceptual language, high-impact research fronts, and specialized community of leaders. The future trajectory of the field hinges on its ability to foster intentional collaboration across this intellectual divide. The most promising breakthroughs will likely emerge from interdisciplinary consortia that leverage profound pathogenic insights such as those from Kapogiannis's lab on neuronal EVs to design the intelligent, targeted therapeutic vectors being engineered in labs like Vader's. It is through such strategic integration that the field can finally unite its two powerful souls to fully master the dual nature of extracellular vesicles.

Top Journals and Highly Cited Articles in Therapeutic and Pathogenic Extracellular Vesicle Research in the Last Decade

An examination of both leading journals and high-impact papers reveals two complementary dynamics shaping the EV research landscape. High-volume, multidisciplinary journals such as the *International Journal of Molecular Sciences* and *Cells* serve as major publication hubs, supporting the rapid growth of the field. However, the studies that have most strongly influenced scientific direction are typically published in specialized, high-prestige journals.

On the therapeutic side, the most influential papers position EVs as platforms for targeted drug delivery. Seminal work by Haney et al. [16] demonstrated the use of exosomes to deliver therapeutics for Parkinson's disease, followed by widely cited studies engineering EVs for cancer drug delivery—including doxorubicin—or for overcoming chemoresistance. These foundational contributions, often published in journals such as *Journal of Controlled Release* and *Biomaterials*, established EV-based therapeutics as a promising translational pathway. In contrast, the pathogenic EV literature is driven by discoveries redefining our understanding of cancer progression. The

most influential study in our dataset, Costa-Silva et al. [17], revealed how pancreatic cancer–derived exosomes precondition the liver for metastasis. Similarly, work by Zhou et al. [19] illuminated EV-mediated vascular remodeling in tumor spread. These landmark papers appeared in top-tier biology and oncology journals, reflecting their transformative impact on disease biology. The field's maturation is further evidenced by the widespread influence of the MISEV guidelines, which rapidly became foundational. Their prominence highlights a collective move toward standardization, methodological rigor, and reproducibility. Overall, EV research operates through a dual structure: broad journals support its expansion, while specialized venues shape its conceptual breakthroughs. Progress now hinges on integrating mechanistic insights from pathogenic studies with the engineering-driven advances in therapeutic applications, ultimately accelerating the development of precise EV-based interventions.

Conclusion

This bibliometric analysis confirms that the "double-edged sword" of extracellular vesicle biology is a structural reality, not just a metaphor. By triangulating publication trends, geographic data, and intellectual networks, we have mapped a field organized into two distinct yet vigorous enterprises: one deconstructing disease pathogenesis and another engineering therapeutic cures. A significant paradigm shift is underway, with therapeutic research now outpacing pathogenic studies a trend embodied by the rising dominance of keywords like 'drug delivery' and the strategic reorientation of leading institutions. The future of EV research hinges on consciously bridging this divide. The most promising breakthroughs will emerge from

interdisciplinary efforts that leverage deep pathogenic insights to design intelligent therapeutic vectors, finally uniting the field's two powerful souls to master its dual nature.

CRediT Authorship Contribution Statement

Soumia Hammadi: Conceptualization, Writing the original draft, Methodology, Data curation. Imane Nouacer: Investigation, Data curation. Benchaa BenKaddour: Writing – review & editing. Dounya Kassimi: Writing – review & editing, Methodology. Walid Hassene HAMRI: Writing – review & editing, Rachid CHAIBI: Writing – review & editing, Project administration.

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Declaration of generative AI and AI-Assisted Technologies in the Manuscript Preparation Process

During the preparation of this manuscript, the author used *ChatGPT* (OpenAI, San Francisco, USA) solely to assist with grammar correction and language refinement. The author reviewed and edited all generated text and takes full responsibility for the content of the manuscript.

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ANNEX

Summary of Key Findings from the Present Bibliometric Analysis

The following Table 06 presents a concise synthesis of this bibliometric analysis, summarizing key insights into *extracellular vesicle (EV)* research across therapeutic and pathogenic domains. It integrates findings on publication trends, leading countries,

institutions, authors, journals, and major research themes. The table is organized around three interpretive axes: implications, trends, and future research agendas to illustrate the field's current dynamics and emerging directions. Overall, Table 06 provides a clear snapshot of the evolving EV research landscape, highlighting its growing translational focus and global scientific engagement.

Table 6: Consolidated Summary of Key Insights in Extracellular Vesicle Research: Therapeutic and Pathogenic Dimensions

Aspects	Findings		Implications		Trends		Future Agenda	
	Therapeutic side	Pathogenic side	Therapeutic side	Pathogenic side	Therapeutic side	Pathogenic side	Therapeutic side	Pathogenic side
Publications	Sharp growth after 2018, reaching a peak in 2024, with exponential expansion in translational studies	Moderate rise peaking around 2021–2022, then stabilizing or slightly declining.	Reflects the field's shift toward applied biomedical innovation and clinical translation.	Indicates consolidation of mechanistic understanding in inflammation, infection, and cancer biology.	Increasing focus on EVs as nanocarriers for drug delivery, regenerative medicine, and immune modulation.	Research driven by disease-related signaling, biomarkers, and pandemic-associated studies.	Strengthen preclinical validation and standardization to advance clinical applications and regulatory approval.	Promote integration of pathogenic insights with therapeutic strategies to build a unified EV framework.
Journals	<i>Journal of Controlled Release, Biomaterials, Advanced Drug Delivery Reviews, Nanomedicine</i>	<i>Nature Cell Biology, Oncogene, Frontiers in Oncology, Cell Reports</i>	Demonstrates strong alignment with biomedical engineering and nanotechnology, focusing on EVs as drug carriers and regenerative agents.	Reflects dominance of cancer biology and neurodegenerative disease research, centering on mechanistic insights into EV-mediated signaling and metastasis.	Rapid expansion of applied EV studies emphasizing delivery systems, biofunctionalization, and clinical translation.	Increasing focus on EVs as biomarkers and mediators of intercellular communication to optimize scalable EV-based progression and inflammation	Broaden interdisciplinary collaboration with material science and pharmacology to optimize scalable EV-based therapies.	Advance cross-disciplinary integration with immunology and neurology to translate mechanistic findings into diagnostic and therapeutic tool
Journals in cross domain	<i>Journal of Extracellular Vesicles, Cells, International Journal of Molecular Sciences</i>		Serves as central platforms for methodological development, standardization, and community coordination (e.g., MISEV2023).		Growing publication volume and global participation emphasizing reproducibility and harmonized reporting standards.		Consolidate global networks for data sharing and methodological unification to ensure consistent EV characterization and reproducibility.	
Countries	China, United States, South Korea, Japan, Italy	China, United States, Germany, Italy, United Kingdom	These countries lead translational EV research through major investments in biotechnology, nanomedicine, and regenerative therapy.	Core contributors to mechanistic and disease-focused studies, especially in oncology and neurodegeneration.	Growth in EV-based drug delivery, immune modulation, and tissue repair.	Focus on EVs as biomarkers for cancer, inflammation, and neurological diseases.	Expand clinical translation via international and interdisciplinary collaboration.	Integrate diagnostic insights with therapeutic innovation through shared research frameworks.
Institutions of research	CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety (China), KAIST (South Korea), Osaka University (Japan), University of North Carolina (USA), University of Turin (Italy)	Weill Cornell Medical College (USA), German Center for Neurodegenerative Diseases – DZNE (Germany), University of Perugia & Istituto Superiore di Sanità (Italy), Cardiff University (UK), CNIO (Spain)	Reflects strong institutional investment in translational biotechnology, nanomedicine, and regenerative therapies aimed at clinical applications of EVs.	Highlights concentration of expertise in mechanistic and disease-specific studies—particularly in oncology, neurodegeneration, and inflammatory disorders.	Growth driven by the convergence of nanotechnology and biomedicine; institutions adopting interdisciplinary, engineering-focused approaches.	Research remains rooted in fundamental cell biology, emphasizing EVs as mediators of disease progression and diagnostic markers.	Encourage cross-institutional collaboration to scale EV-based therapeutic platforms, integrating engineering, molecular biology, and clinical science.	Strengthen translational pathways linking mechanistic discoveries to applied interventions through interdisciplinary and cross-border initiatives. biology, and clinical science.
Authors	The field includes leading experts and emerging researchers, such as Giovanni Camussi	Dimitrios Kapogiannis (National Institute on Aging), Héctor Peinado (CNIO, Spain)	Represent leaders advancing EVs as therapeutic tools for regeneration, wound healing, and targeted drug delivery. Their	Illustrate the field's mechanistic focus on neurodegeneration, inflammation, and cancer metastasis, using EVs as	Growing collaboration between regenerative medicine, bioengineering, and	Emphasis on EV-mediated communication in tumor microenvironments and neuroinflam	Expand cross-disciplinary integration with molecular biology and immunology to develop	Foster translational links between pathogenic understanding and therapeutic application,

	(University of Turin), Michael Chopp (Henry Ford Hospital), Pieter Vader (UMCUtrecht)		work translates EV biology into clinically relevant nanomedicine and gene therapy applications.	diagnostic biomarkers and mediators of disease progression.	nanotechnology to enhance EV design and functionality.	matory pathways, with strong citation impact in diagnostic and mechanistic studies.	standardized, safe, and scalable EV-based therapeutic platforms	promoting shared research models and inter-laboratory collaborations.
Topic of research	mRNA Vaccines and Lipid Nanoparticle Innovations (FWCI 2.63); EV-based Drug Delivery and Gene Therapy; Wound Healing and Tissue Regeneration	Cerebrospinal Fluid Biomarkers in Alzheimer's Disease (FWCI 2.80); Circulating Tumor DNA as a Diagnostic Tool (FWCI 1.57); Exosome-mediated Metastasis and Fibrosis Mechanisms	Indicates a translational and bioengineering-driven focus on utilizing EVs as delivery platforms and regenerative mediators for clinical applications.	Reveals a strong mechanistic and diagnostic focus, emphasizing EVs as mediators and biomarkers of neurodegenerative and oncogenic processes.	Rapid growth in EV engineering, including nucleic acid delivery systems, regenerative medicine, and nanomedicine convergence.	Increasing concentration on neurodegeneration and cancer biology, particularly in understanding EV-mediated communication within the tumor microenvironment and neural pathways.	Scaling clinical translation through safety optimization, standardization of EV production, and cross-disciplinary integration with nanotechnology and immunotherapy.	Expansion toward multi-omics integration and translational biomarker validation to support early disease detection and therapeutic intervention based on EV signaling.
Key words	"drug delivery", "wound healing", "immune modulation", "regenerative medicine", "blood-brain barrier", "gene therapy"	"Biological markers", "signal transduction", "cell proliferation", "tumor microenvironment", "gene expression regulation", and pathological state: "inflammation", "fibrosis", "carcinogenesis",	Reflects a translational and application-oriented focus, emphasizing EVs as therapeutic vectors, delivery platforms, and regenerative tools.	Highlights a mechanistic and diagnostic orientation, focusing on EVs as mediators of disease communication and biomarkers of pathological states.	Research increasingly integrates nanotechnology, gene editing, and tissue repair strategies, demonstrating convergence between molecular biology and clinical bioengineering.	Strong emphasis on decoding EV-mediated intercellular signaling and its implications for tumor progression, fibrosis, and chronic inflammatory diseases.	Advance towards large-scale clinical translation, biomanufacturing optimization, and safety profiling of EV-based therapeutics, particularly in regenerative and neurological contexts.	Deepen multi-omics investigations of EV cargo, expand diagnostic applications, and explore therapeutic blockade of pathogenic EV pathways to mitigate disease progression.