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CRISPR-Based Gene Therapy and Bioethics: A Bibliometric Mapping and Systematic Literature Review (2016–2026)

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ABSTRACT

This study integrates bibliometric mapping and a systematic literature review (SLR) to examine CRISPR-related technologies, therapeutic applications, and bioethical issues. A Scopus search on 9 May 2026 identified 275 records; predefined limits and abstract screening yielded 60 journal-source publications from 2016–2026. Biblioshiny (bibliometrix 5.0) was used to examine annual scientific production, country participation, citations, keyword co-occurrence, and thematic mapping. The highest annual output was nine publications in 2023. The United States (43), Australia (17), Spain (16), and China (13) had the highest country-production values. Gene editing, human, and gene therapy occupied basic-theme positions. Descriptive primary-focus coding of the 60 records identified ethics, governance, and public perceptions (36), therapeutic applications (17), editing mechanisms (4), and diagnostics or infectious disease (3). Reported challenges included off-target activity, delivery, and immunogenicity, while ethical issues involved germline editing, enhancement, public acceptance, and equitable access. Integrating these strands connects mapped terminology to specific technological and normative questions. The conclusions concern the selected corpus, not the clinical effectiveness or worldwide maturity of CRISPR technology.

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INTRODUCTION

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) systems enable targeted genome modification and have stimulated research on therapeutic applications, including newer approaches to precision editing (Mengstie & Wondimu, 2021; Hryhorowicz et al., 2023). Their use also raises questions of editing specificity, biological safety, delivery, and the ethical boundaries of human genome modification (Brokowski & Adli, 2019; Vassena et al., 2016). These

technical and normative questions warrant analysis alongside the development of the research literature.

Bibliometric studies have mapped the expanding literature on CRISPR and gene editing. Dandoti and Ansari (2023) examined productive researchers, sources, countries, and research trends in Scopus-indexed CRISPR publications, while Wei et al. (2022) investigated research activity, collaboration, innovation, and regulation in a broader gene-editing literature. Such analyses identify where attention is concentrated, but publication and keyword indicators alone cannot establish what the underlying studies conclude about therapy or bioethics.

Conversely, focused evidence syntheses have examined specific questions, such as public attitudes toward genetic engineering (Ramos et al., 2023) and CRISPR-Cas9 approaches in cancer therapy (Rehman & Abbas, 2026). These reviews provide substantive detail, but they do not directly connect their findings with the conceptual structure and publication patterns of a corpus deliberately selected at the intersection of CRISPR, therapeutic applications, and ethical considerations.

The present study addresses this gap by combining bibliometric analysis with a systematic literature review (SLR). Bibliometric mapping describes publication activity, geographical participation, citation patterns, and co-occurring research terms; qualitative synthesis examines the applications, technical limitations, and ethical arguments discussed in the selected publications. The integration is interpretive: keyword relationships guide examination of the literature rather than serving as direct evidence of clinical effectiveness or causal thematic change.

The conceptual framework therefore comprises two complementary strands applied to a common corpus: quantitative mapping of research patterns and qualitative classification of technological, therapeutic, and bioethical topics. Their comparison supports a more focused account of how genome-editing applications and ethical questions appear within the same publication landscape. The scope is limited to the records captured by the stated search strategy rather than all worldwide CRISPR scholarship.

The study aims to identify temporal, geographical, and conceptual patterns and to relate these patterns to substantive issues described in the selected literature. It addresses two research questions:

RQ1. What publication, geographical, and conceptual patterns characterize the selected CRISPR, gene therapy, and bioethics literature during 2016–2026?

RQ2. How do the reported applications, technical challenges, and bioethical issues relate to the themes identified through bibliometric mapping?

RESEARCH METHODS

This study combined quantitative bibliometric mapping with a systematic literature review of a shared set of Scopus-indexed publications. Bibliometric indicators were used to describe scientific production and conceptual relationships, while qualitative synthesis examined therapeutic applications, technical challenges, and bioethical considerations. The two strands were compared to interpret the substantive meaning of the mapped research themes.

Records were retrieved from Scopus on 9 May 2026 for the publication period 2016–2026 (Table 1). The search used three TITLE-ABS-KEY term groups covering genome editing, therapeutic applications, and ethical considerations, with OR within groups and AND between groups. The full query and database filters are provided in Table 2. The search strategy was applied to Scopus bibliographic records, which also supplied the metadata used for bibliometric mapping (Donthu et al., 2021).

Table 1. Overview of search and selection

Description	Condition
Initial Scopus search	275 records; three TITLE-ABS-KEY term groups (full expression in Table 2)
After applying database limits	66 records; publication year, language, journal source, final stage and open-access limits
Date of data collection	May 9, 2026
Years covered	2016–2026
Source type	Journal
Publication Stage	Limited to final
Language	Limited to English

The original Scopus query returned 275 records; the year, English-language, journal-source, final-stage, and open-access limits retained 66. Historical abstract-level relevance screening excluded six records, yielding the fixed 60-publication corpus (Figure 1). The four descriptive categories in Table 5 were applied after inclusion, without repeating screening or changing the Biblioshiny dataset. The 2026 observation ended on 9 May.

Table 2. Search string used in the Scopus database

Database	Search String
Scopus	(TITLE-ABS-KEY ("CRISPR" OR "CRISPR-Cas9" OR "gene editing" OR "genome editing" OR "genetic modification" OR "genetic engineering") AND TITLE-ABS-KEY ("disease treatment" OR "disease therapy" OR "gene therapy"

OR "therapeutics") AND TITLE-ABS-KEY ("human enhancement" OR "human engineering" OR "designer babies" OR "ethical issues" OR "bioethics")) AND PUBYEAR > 2015 AND PUBYEAR < 2027 AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (SRCTYPE , "j")) AND (LIMIT-TO (PUBSTAGE , "final")) AND (LIMIT-TO (OA , "all"))

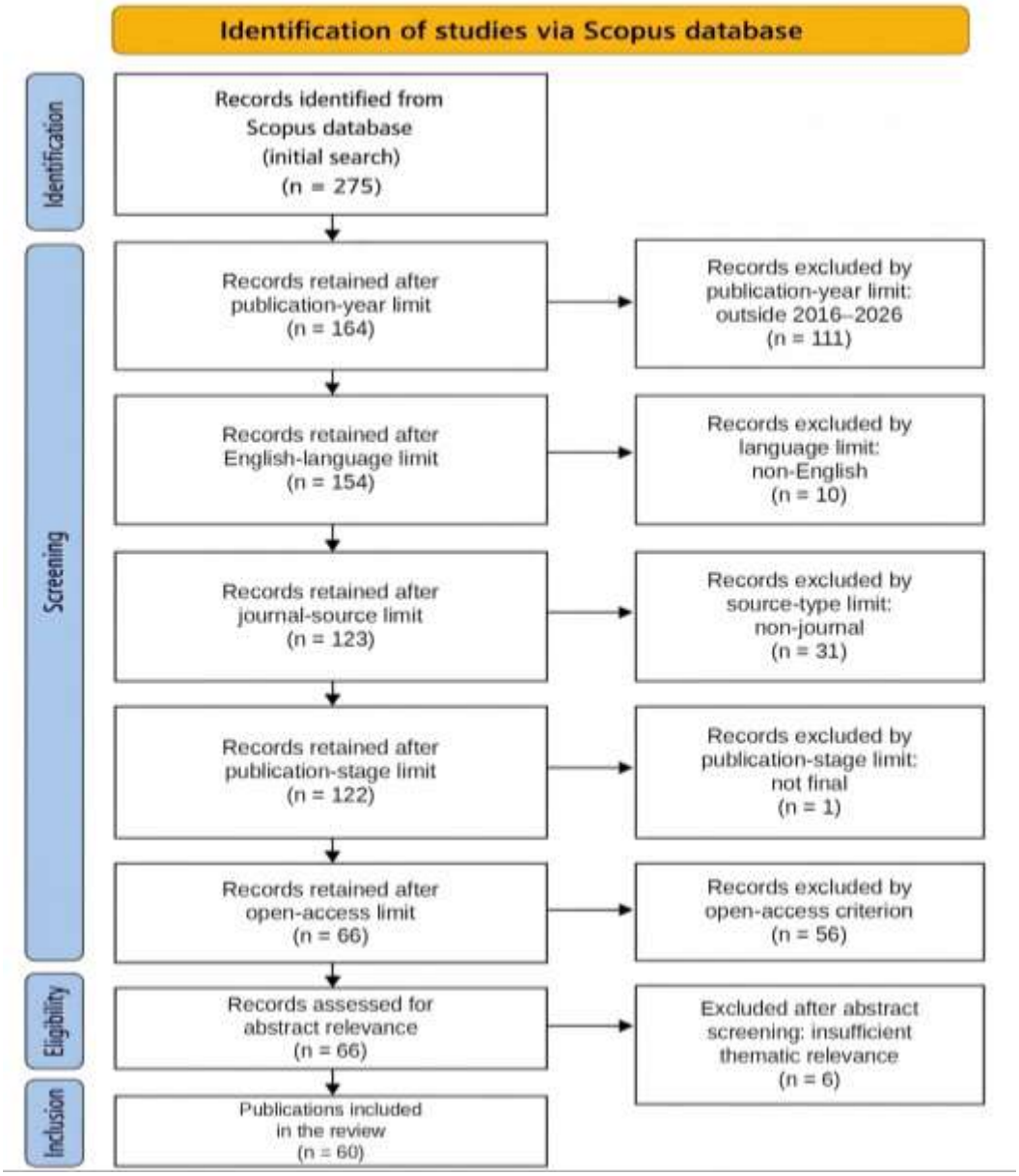


Figure 1. PRISMA flow diagram of the study selection process

Bibliometric analysis was conducted using Biblioshiny, the web-based interface of the bibliometrix R package (version 5.0). The indicators examined included annual scientific production, relevant sources, country scientific production, global citations, international co-authorship, keyword co-occurrence, and thematic mapping. The reported values and figures reflect the Scopus metadata available when records were retrieved on 9 May 2026. As Scopus updates its

coverage, bibliographic metadata, and citation counts over time, a later search using identical terms and filters may yield different records and bibliometric indicators. Country-production figures may include contributions from multiple national affiliations for the same publication; keyword links describe co-occurrence, and thematic quadrants are interpreted through centrality and density. These indicators were not used as measures of clinical efficacy or study quality.

Table 3. Inclusion and exclusion criteria

Criteria	Condition	Exclusion
Timeline	2016–2026 (11 calendar years; 2026 partial)	< 2016
Publication Stage	Final	In-press
Source Type	Journal	Non-journal
Language	English	Non-English
Accessibility	All open access	Not open access

Supplementary Table S1 summarizes bibliographic identity, document type, subject focus, applications, and ethical questions for the fixed corpus. Post-selection coding assigned each publication one descriptive primary-focus label based on the dominant research or discussion subject in its title, abstract, and available source summary; secondary topics were described but not counted again. Contextual papers on adjacent technologies or broader therapies and ethics are identified in Table S1 and were not used as direct evidence of CRISPR efficacy or safety. Reviews, editorials, notes, and letters were not treated as independent clinical trials. The categories were compared qualitatively with bibliometric themes, not statistically assigned to thematic-map clusters.

The two analyses were integrated by comparing the thematic positions of indexed terms with findings and arguments from the corresponding groups of publications. This comparison was designed to interpret what bibliometric themes represent in substantive terms; it did not treat keyword prominence as evidence of treatment effectiveness, study quality, or longitudinal causal change.

The identification, database filtering, relevance screening, and inclusion stages are summarized in a PRISMA-informed flow (Figure 1) (Moher et al., 2009). The journal-source filter concerns the publication venue; it does not restrict the corpus to original research articles. Accordingly, review articles and scholarly commentaries were interpreted according to their evidence type.

RESEARCH RESULT

The selected corpus comprised 60 publications from 52 journal sources, covering 2016 through 9 May 2026. Bibliometric results describe production, geographical representation, and thematic structure (RQ1). Document-level summaries then contextualize potential applications, technical constraints, and bioethical questions (RQ2), distinguishing directly relevant CRISPR evidence from broader scientific or ethical background.

RQ1. Publication Patterns, Geographic Participation, and Conceptual Structure

Publication output varied rather than growing steadily, from two records in 2020 to a peak of nine in 2023 (Figure 2). The 2026 count of two covers only the months preceding 9 May. The annual growth rate of −8.76% in Table 4 reflects the change between 2016 and this incomplete endpoint, and should not be interpreted as a sustained decline in global CRISPR research. The average document age was 5.55 years and mean citations per document were 41.32 at retrieval (Table 4). These descriptive averages do not imply uniform research impact or clinical effectiveness.

Table 4. Main bibliometric information

Description	Results
Timeframe	2016–2026
Sources	52
Documents	60
Annual Growth Rate %	-8.76
Document Average Age	5.55
Average citations per doc	41.32
International co-authorships %	33.33

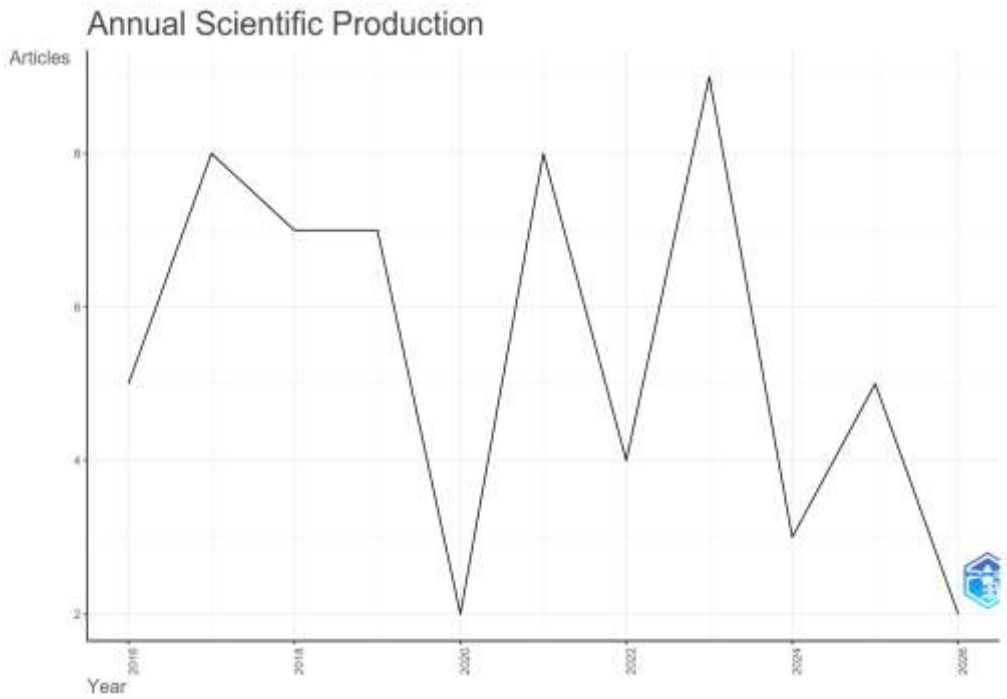


Figure 2. Annual scientific production of CRISPR research

The 60 records were spread across 52 journal sources; eight sources each contributed two publications (Figure 3). This dispersion reflects the study's combination of molecular, clinical, and ethical subject areas, rather than a concentration in a small number of journals. The contributions include Bioethics, British Medical Bulletin, The CRISPR Journal, EMBO Reports, Frontiers in Genetics, Frontiers in Microbiology, Human Gene Therapy, and Progress in Retinal and Eye Research.

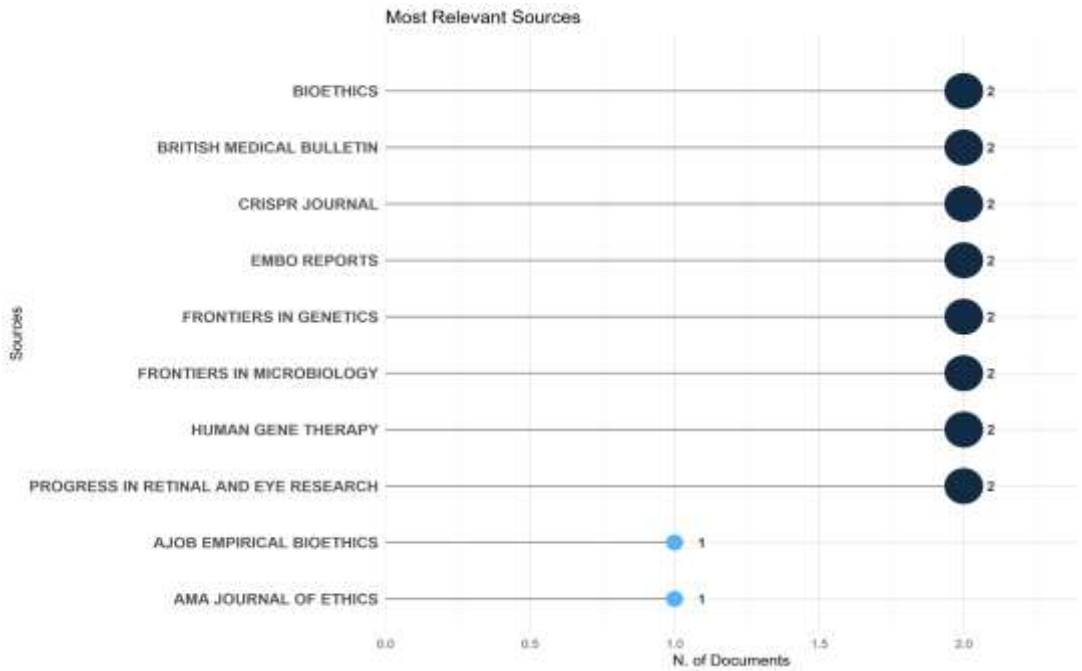


Figure 3. Most relevant sources in CRISPR research

The United States had the highest country-production value (43), followed by Australia (17), Spain (16), and China (13) (Figure 4). Country-production values are not mutually exclusive article totals because publications with authors from different countries may contribute to more than one country. International co-authorship accounted for 33.33% of the corpus (Table 4), indicating an aggregate level of cross-national co-authorship. Figure 4 is a country-production visualization, not a bilateral collaboration network: the reported outputs do not provide country-pair links, connection strengths, or network centrality, so particular partnerships cannot be ranked from these indicators.

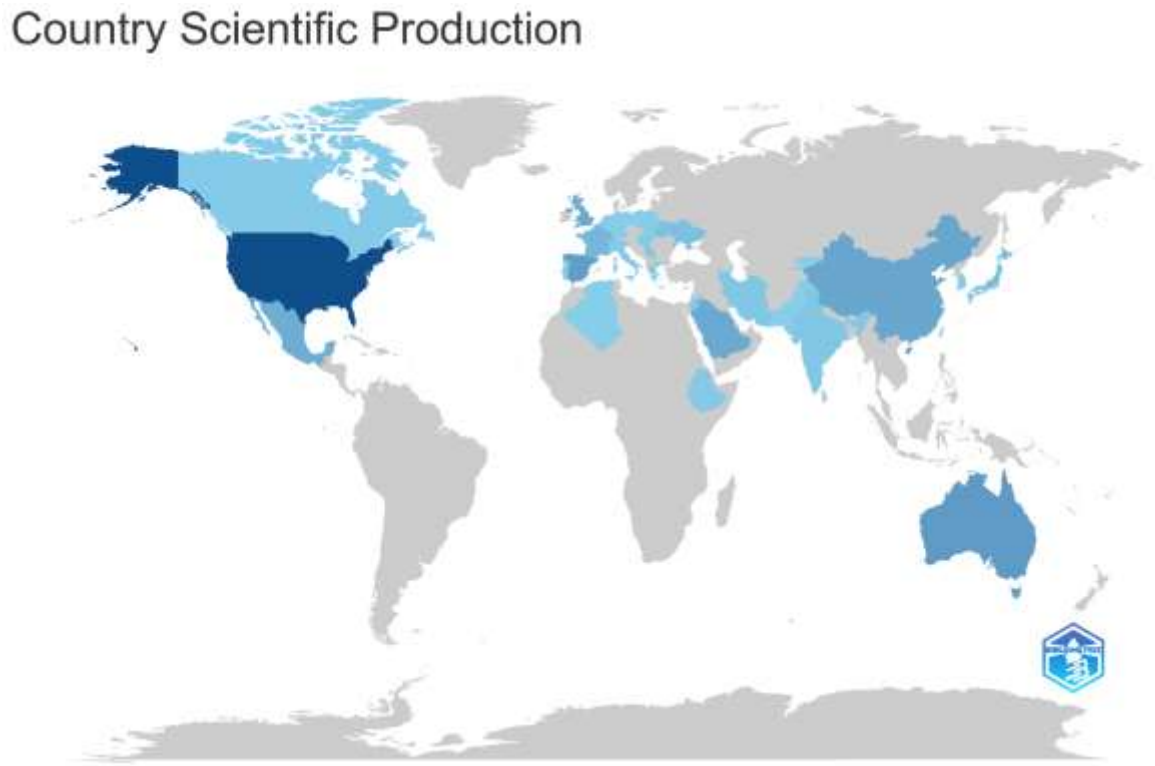


Figure 4. Scientific production by country

For the Scopus retrieval dated 9 May 2026, the leading global citation values within the selected corpus were Volarevic et al. (2018; 744), Mengstie and Wondimu (2021; 436), and Brokowski and Adli (2019; 202) (Figure 5). Volarevic et al. examine stem-cell safety and ethics more broadly; citation visibility is therefore not equivalent to CRISPR-specific clinical evidence.

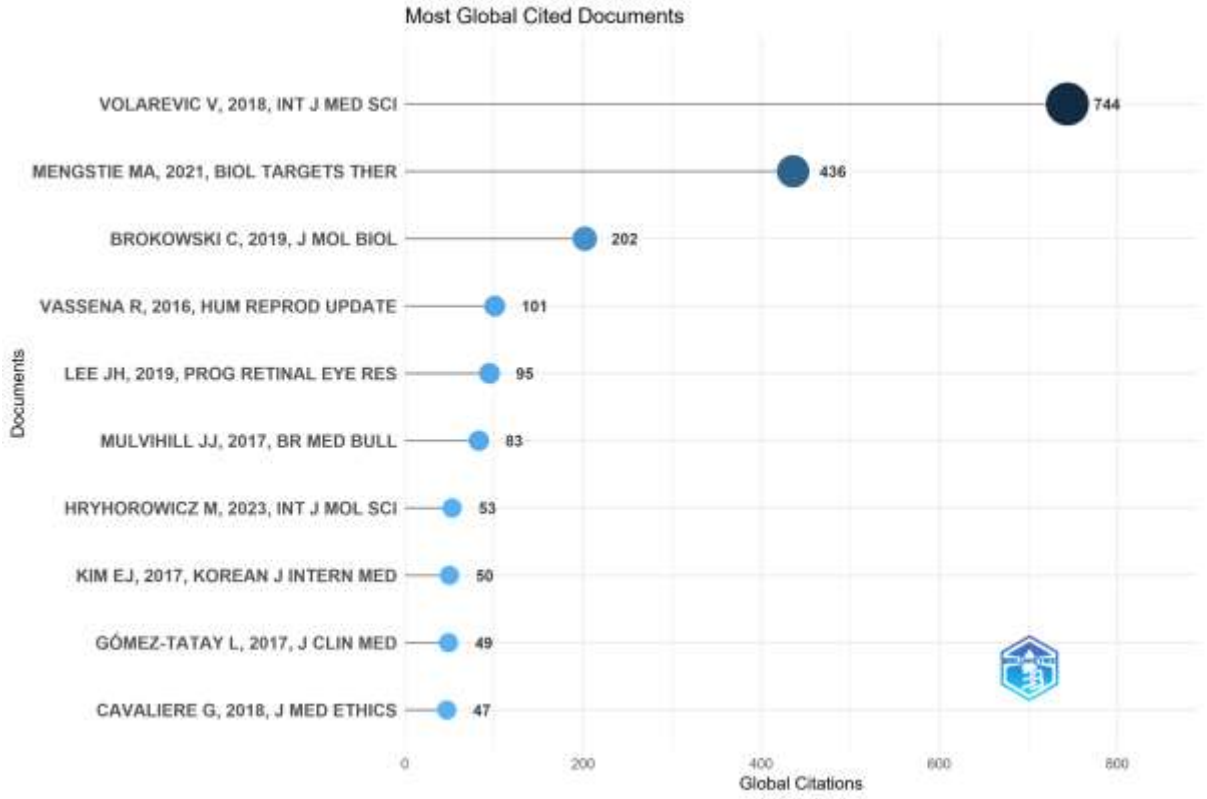


Figure 5. Most cited documents globally

Figure 6 shows a large red group linking gene editing, gene therapy, human/humans, and ethics, a blue group with CRISPR-Cas and related technical terms, and a smaller green human-genome group. The links represent term co-occurrence, not clinical evidence; indexing variants such as human/humans can affect the visual network.

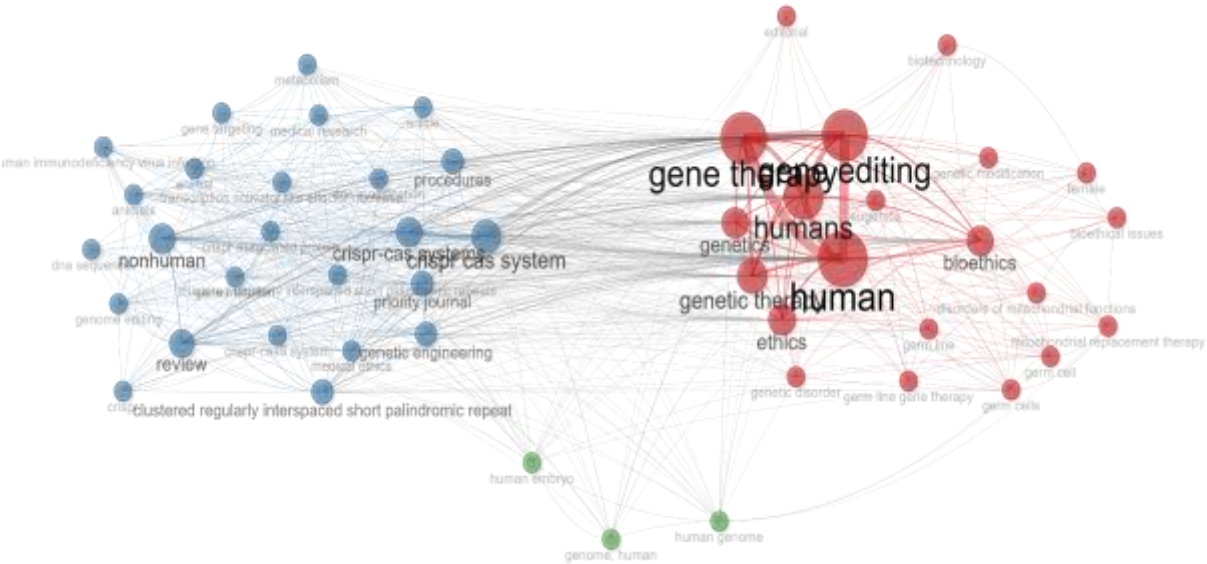


Figure 6. Keyword co-occurrence network

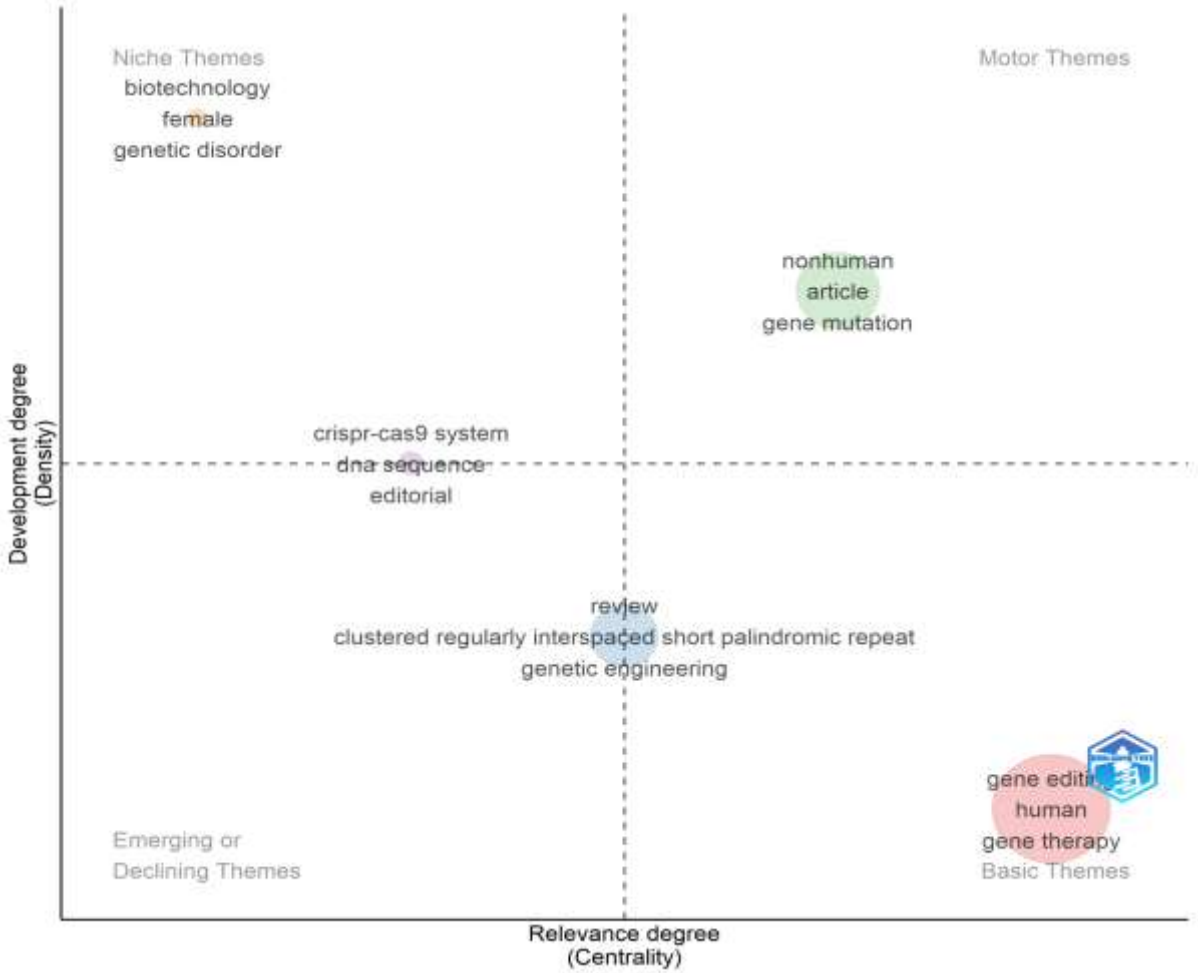


Figure 7. Thematic map

Figure 7 places gene editing, human, and gene therapy among basic themes, characterized here by relatively high centrality and lower density. Biotechnology, female, and genetic disorder occur in the niche-theme quadrant, with stronger within-cluster development but weaker connections to other mapped terms. The motor-theme group includes nonhuman, article, and gene mutation; generic indexing vocabulary warrants caution when interpreting that position. CRISPR-Cas9 system, DNA sequence, and editorial lie near the density boundary, whereas review and genetic engineering occur close to the centrality division, so small positional differences should not be overinterpreted. The map represents thematic organization in the selected records, not longitudinal change or evidence of therapeutic maturity.

RQ2. Applications, Technical Challenges, and Bioethical Issues in Relation to Mapped Themes

For the descriptive synthesis, the 60 historically selected records were assigned one primary-focus label each: ethics, governance, and public perception (36); therapeutic and disease-related applications (17); editing technologies and mechanisms (4); and diagnostics and infectious

disease (3) (Table 5). These categories characterize the principal subject of each publication, not four mutually exclusive domains in the broader literature or counts of trials and successful treatments. The supplementary matrix records secondary topics and identifies publications used only as contextual literature; those items do not substantiate CRISPR-specific intervention claims.

Table 5. Descriptive primary-focus coding of the 60 publications

Primary Focus (Mapped Records)	Illustrative Publications	Substantive Issues
Ethics, governance and public perception (n = 36)	Brokowski & Adli (2019); Vassena et al. (2016); Ramos et al. (2023); Rueda et al. (2024)	Heritable modification, public perceptions, therapy/enhancement boundary, governance, and access to interventions.
Therapeutic and disease-related applications (n = 17)	Cannon et al. (2021); Rehman & Abbas (2026); Motta et al. (2017)	Disease-related gene editing, models, and translational prospects; some other records offer contextual therapeutic background rather than direct CRISPR evidence.
Editing technologies and mechanisms (n = 4)	Hryhorowicz et al. (2023); Kim et al. (2017); Mengstie & Wondimu (2021)	CRISPR/Cas systems, genome-editing mechanisms and technical limitations, including precision and off-target activity.
Diagnostics and infectious disease (n = 3)	Tripathi et al. (2023); El Ouar & Djekoun (2021)	CRISPR-based diagnosis and infection-oriented applications and directions.

The technology and therapy literature documents both application opportunities and unresolved limitations. Mengstie and Wondimu (2021) and Hryhorowicz et al. (2023) discuss mechanisms and precision-editing approaches, while Cannon et al. (2021) examines challenges in hematopoietic stem-cell targeting. Tripathi et al. (2023) address infectious-disease diagnostics and therapeutics. Across these differently designed publications, delivery, off-target alterations, and immunogenicity recur as concerns; this synthesis does not combine them into treatment-effect estimates.

Ethical and governance-oriented publications discuss the boundary between therapeutic correction and enhancement, germline modification, public acceptance, regulatory oversight, and access. Vassena et al. (2016) and Brokowski and Adli (2019) address safety and ethical questions associated with human genome editing; Ramos et al. (2023) synthesize public perceptions, while Rueda et al. (2024) foreground affordability. These distinct arguments provide a substantive context for the proximity of ethical and human-related terms in the bibliometric networks.

The combined reading separates the prominence of mapped terms from the evidential content of the publications. CRISPR mechanism and application reviews help explain the gene-editing and gene-therapy themes, while studies of germline editing, public perceptions, and equitable access clarify the ethical vocabulary. Contextual articles dealing with non-CRISPR technologies are used only to frame related debates, not to establish CRISPR-specific mechanisms or clinical outcomes. Accordingly, Table 5 is an interpretive classification of this corpus and not an estimate of treatment success or a statistical assignment of every article to a thematic-map cluster.

DISCUSSION

The bibliometric and literature-synthesis strands answer different questions. Dandoti and Ansari (2023) used a substantially broader CRISPR research dataset to characterize scientific production and leading contributors, whereas the present deliberately intersecting search captures a smaller set linking editing, therapy, and ethics. Wei et al. (2022) similarly mapped innovation and regulation in gene editing across a wider literature. Their broader maps help contextualize our publication and geographic indicators, but different search populations mean that direct comparisons of productivity or growth rates would be inappropriate. The added contribution here is to connect mapped terms with the types of technical evidence and normative arguments represented in the selected documents.

The prominence of ethical and governance themes must be understood in relation to the search design, which required therapeutic and ethical terminology alongside gene-editing terms. Their co-occurrence therefore does not by itself demonstrate longitudinal convergence. This interpretation differs from topic-specific reviews such as Ramos et al. (2023), which synthesize public perceptions, and Rehman and Abbas (2026), which examine cancer-directed CRISPR approaches. Taken together, these studies show why quantitative mapping and study-level reading are complementary: the former locates concepts, while the latter differentiates empirical applications from ethical argument and broader contextual literature.

The country-production ranking points to broad multinational participation, but the 33.33% international co-authorship indicator does not identify particular country pairs or partnership leaders. Likewise, global citations measure scholarly visibility; highly cited ethical discussion or stem-cell research should not be treated as a measure of CRISPR treatment quality. The thematic map places gene editing and gene therapy in basic-theme positions, yet indexed terms such as article and nonhuman are shaped partly by metadata conventions. These patterns support interpretation of the selected literature but not claims of clinical maturity. Limitations include

coverage of one database, the specified English-language and open-access filters, the partial 2026 period, and the inclusion of heterogeneous publication types. Bibliometric network displays are also sensitive to term selection and mapping settings. Accordingly, the study makes descriptive rather than causal or treatment-effect inferences.

CONCLUSION

For RQ1, the 60-publication Scopus corpus contained 52 journal sources and showed fluctuating output, peaking at nine publications in 2023. Thematic mapping emphasized gene editing, gene therapy, human-related terminology, and ethics, while country-production values were highest for the United States, Australia, Spain, and China. For RQ2, the descriptive synthesis identified therapeutic and diagnostic applications, ongoing precision and delivery challenges, and ethical concerns involving heritable editing, enhancement, regulation, and access. Combining these perspectives clarifies the substantive issues associated with bibliometric themes without treating keyword prominence or citations as evidence of clinical effectiveness. The findings concern the selected search corpus, not the entirety of worldwide CRISPR research.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

A. Yuliana: supervision, resources, and validation. **F. Al Majid:** conceptualization, methodology, software, formal analysis, resources, project administration, visualization, data curation, writing – original draft, and writing – review & editing. **A. A. Pratiwi:** supervision, conceptualization, and validation.

DECLARATION OF THE USE OF AI

During manuscript preparation and revision, the authors used ChatGPT and Gemini to assist with language editing, literature organization, and preparation of descriptive summaries. AI-generated suggestions were treated as drafting aids rather than independent research evidence. The authors are responsible for verifying citations, source interpretations, tabulated data, and the final manuscript.

DATA AVAILABILITY STATEMENT

The study-level bibliographic characteristics and primary-focus classifications are provided in Supplementary Table S1. Bibliometric indicators reflect the Scopus retrieval on 9 May 2026.

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