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KRAS-Targeting Agents in Cancer: A Bibliometric Analysis of Global Research Trends and Emerging Hotspots from 2006 to 2026

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Abstract

Purpose

To characterize the global research landscape, collaboration patterns, intellectual structure, and emerging hotspots of KRAS-targeted therapy in cancer using bibliometric and science-mapping methods.

Methods

Web of Science Core Collection records from 2006 to 2026 were analyzed after restriction to articles and reviews. Bibliometrix/Biblioshiny, VOSviewer, R, and Microsoft Excel were used to evaluate annual publication output, citation patterns, country and institutional activity, source distribution, author productivity, co-occurrence networks, co-citation structure, co-authorship, and trend topics.

Results

The final dataset included 3,265 publications, comprising 2,675 articles and 590 reviews, distributed across 723 sources and citing 88,334 references. Annual publication output increased gradually through the 2010s and accelerated after 2020, reaching its highest level in 2025. Country-affiliation occurrence frequency was highest for the USA and China, while country-level citation impact was led by the USA. Major sources included Cancer Research, Journal of Clinical Oncology, Journal of Thoracic Oncology, Molecular Cancer Therapeutics, and Annals of Oncology. Trend-topic and co-occurrence analyses showed a temporal shift from indirect KRAS-targeting approaches, pathway inhibition, synthetic lethality, and preclinical tumor models toward KRAS G12C, AMG 510, KRAS inhibition, efficacy, KRAS G12D, resistance, and molecular targeted therapy.

Conclusion

KRAS-targeted therapy research has evolved from a historically pathway-centered and indirect-targeting literature into a rapidly expanding precision-oncology field. Current bibliometric patterns highlight direct mutant KRAS inhibition, resistance biology, allele-specific targeting beyond G12C, and clinically oriented molecular targeted therapy as major research frontiers. These bibliometric findings should be interpreted as indicators of research activity and intellectual structure rather than evidence of therapeutic efficacy.

Introduction

Kirsten rat sarcoma viral oncogene homolog (KRAS) is one of the most important oncogenic drivers in human cancer and has major relevance across lung, colorectal, pancreatic, and other solid tumors (Lee, 2022). For many years, KRAS was considered a difficult therapeutic target because its relatively smooth

molecular surface lacks well-defined binding pockets for small-molecule inhibitors, while its picomolar affinity for Guanosine Triphosphate (GTP) and Guanosine Diphosphate (GDP) makes competitive nucleotide displacement exceptionally challenging. This combination of biological importance and pharmacological intractability established KRAS as a central example of an oncogenic target that was biologically compelling but therapeutically elusive (Cox et al., 2014).

Consequently, early therapeutic strategies focused on indirect approaches, including farnesyltransferase inhibition and downstream pathway blockade (Cox et al., 2015). Although these approaches advanced understanding of KRAS biology, they failed to produce durable, broadly effective KRAS-selective therapies. This changed with the discovery of covalent allosteric inhibitors targeting the switch-II pocket of KRAS G12C, providing the first practical strategy for direct mutant KRAS inhibition (Ostrem et al., 2013).

Subsequent preclinical and translational studies advanced this concept toward clinical development. Janes et al. (Janes et al., 2018) described a covalent G12C-specific inhibitor with antitumor activity in KRAS-mutant models, while Canon et al. (Canon et al., 2019) reported the activity of AMG 510 and its immune-related effects. Hallin et al. (Hallin et al., 2020) further characterized MRTX849 and linked molecular context to therapeutic susceptibility.

Clinical translation accelerated after direct KRAS G12C inhibition showed activity in patients with advanced solid tumors and KRAS G12C-mutant NSCLC (Hong et al., 2020) (Skoulidis et al., 2021). Subsequent studies of adagrasib, comparative evaluation of sotorasib, and acquired resistance expanded the field beyond proof of targetability toward optimization of therapeutic efficacy and understanding mechanisms of resistance (Awad et al., 2021) (Jänne et al., 2022) (de Langen et al., 2023).

This study is the first bibliometric analysis focused specifically on pharmacological KRAS inhibitors. It aimed to characterize global publication trends, collaboration patterns, intellectual structure, and emerging research hotspots in KRAS-targeted drug development between 2006 and 2026 using bibliometric performance analysis and science mapping.

Material and methods

Data source and search strategy

The Web of Science Core Collection was used as the bibliographic data source because of its standardized citation metadata and compatibility with established bibliometric workflows. The search was conducted on 2 July 2026 and covered publications from 2006 to 2026. Records were exported in BibTeX format with full records and cited references for subsequent analysis.

The following topic-field search strategy was applied: TS=((KRAS OR "K-RAS" OR "K RAS" OR "Kirsten rat sarcoma" OR "KRASG12C" OR "KRAS G12C" OR "KRASG12D" OR "KRAS G12D") AND (inhibitor* OR

inhibition OR "targeted therapy*" OR "molecular targeted therapy*" OR "farnesyltransferase inhibitor*" OR "synthetic lethal*" OR "synthetic lethality" OR "gene therapy" OR degrader* OR PROTAC OR sotorasib OR adagrasib OR "AMG 510" OR MRTX849 OR divarasib OR "GDC-6036" OR olomorasib OR "LY3537982" OR JDQ443 OR D-1553 OR glecirasib OR "RMC-6236" OR "RAS(ON)" OR "RAS ON" OR "pan-KRAS" OR "pan-RAS") AND (cancer OR tumor* OR tumour* OR neoplasm* OR carcinoma* OR oncology)).

Eligibility criteria and data cleaning

Only articles and reviews were included in the final analysis. Meeting abstracts and other non-article/review document types were excluded. English-language records were retained to support consistent keyword and citation analysis. Synonymous terms were interpreted cautiously during thematic interpretation, particularly KRAS, K-RAS, K RAS, KRAS G12C, and KRASG12C variants.

Bibliometric and science-mapping analysis

Bibliometric performance analysis and science mapping were conducted using Bibliometrix/Biblioshiny in R and VOSviewer. These tools were selected because Bibliometrix provides a reproducible R-based framework for comprehensive science mapping, VOSviewer supports network visualization and clustering, and the combined approach is consistent with established bibliometric methodology (Donthu et al., 2021, Aria and Cuccurullo, 2017, van Eck and Waltman, 2010).

Performance indicators included annual publication output, average citation patterns, country-affiliation occurrence frequency, country citation impact, institutional productivity, author-string productivity, source distribution, and globally cited documents. Science-mapping analyses included keyword co-occurrence, trend-topic analysis, collaboration-network visualization, cited-author co-citation analysis, and author co-authorship analysis. In VOSviewer maps, node size reflects the weight of an item within the network; links represent relationships between items, and colors indicate clusters generated by the software.

PRISMA-style reporting

The study-selection process is summarized in a PRISMA-style flow diagram showing database identification, document-type filtering, and final inclusion (Fig. 1).

Results

Study selection and dataset characteristics

The final dataset included 3,265 publications indexed from 2006 to 2026 after restriction to articles and reviews (Table 1). These records were distributed across 723 sources and cited 88,334 references. Document-type reporting was consolidated into 2,675 articles and 590 reviews.

The author network included 22,537 authors, with 45 single-authored documents, an average of 11.5 co-authors per document, and 29.19% international co-authorship. These findings indicate that KRAS-targeted therapy has evolved into a large, collaborative body of oncology literature rather than remaining in a small, emerging niche.

Table 1
Main bibliometric information and consolidated document types for the included article/review dataset.

Characteristic	Value
Timespan	2006–2026
Sources	723
Documents	3,265
Annual growth rate	17.41%
Document average age	5.1 years
Average citations per document	41.2
References	88,334
Keywords Plus	4,765
Author keywords	4,810
Authors	22,537
Single-authored documents	45
Co-authors per document	11.5
International co-authorship	29.19%
Articles	2,675
Reviews	590

Annual scientific production and citation trajectory

Annual scientific production increased gradually from 2006 through the 2010s and accelerated after 2020, reaching its highest level in 2025 (Fig. 2). The apparent decrease in 2026 should be interpreted cautiously because the search year may be incomplete, and database indexing for the calendar year may not yet be finalized.

Average article citations per year showed peaks in 2009 and 2020, respectively, whereas the decline in the most recent years likely reflects citation lag rather than lower scientific relevance (Fig. 3).

Country-level activity and citation impact

Country-level activity was led by the USA and China, followed by Germany, Japan, Italy, South Korea, Spain, the UK, France, and India (Table 2; Fig. 4). Country production values in this analysis represent country-affiliation occurrence frequency rather than unique publication counts.

Country production over time showed sustained USA leadership and a steep recent rise in China, while Germany, Japan, and Italy contributed smaller but consistent trajectories (Fig. 5). Citation impact was led by the USA, followed by China, Germany, Japan, and the UK, indicating that production activity and citation influence were related but not identical across countries.

Table 2
Leading countries by country-affiliation occurrence frequency and citation impact.

Country	Country-affiliation occurrence frequency	Total citations	Average article citations
USA	7,922	71,923	63.3
China	4,930	13,977	19.4
Germany	1,038	4,263	38.4
Japan	1,036	3,891	18.6
Italy	851	2,189	24.9
South Korea	669	2,238	20.5
Spain	636	1,467	29.9
UK	595	2,891	36.6
France	526	1,226	31.4
India	436	652	9.9

Source, affiliation, and author-string productivity

The most frequent publication sources were Cancer Research, Journal of Clinical Oncology, Journal of Thoracic Oncology, Molecular Cancer Therapeutics, and Annals of Oncology (Table 3a). The leading affiliations were major cancer centers, translational oncology programs, and industry-linked research environments, including the University of Texas MD Anderson Cancer Center, Memorial Sloan Kettering Cancer Center, Dana-Farber Cancer Institute, University of California San Francisco, and Shanghai Jiao Tong University (Table 3b).

The most frequent author strings were dominated by common surnames and initials (Table 3c). Because abbreviated author strings can merge multiple individuals who share the same surname and initials,

these results should be interpreted as indexed name-string frequencies rather than definitive individual-author rankings without manual disambiguation.

Table 3
a. Most relevant publication sources in KRAS-targeted therapeutic research, ranked by the number of included records.

Rank	Source	Documents
1	Cancer Research	470
2	Journal of Clinical Oncology	175
3	Journal of Thoracic Oncology	126
4	Molecular Cancer Therapeutics	104
5	Annals of Oncology	99
6	Journal of Medicinal Chemistry	60
7	Cancer Science	57
8	Nature Communications	57
9	Clinical Cancer Research	55
10	Oncogene	52

Table 3
b. Most relevant affiliations in KRAS-targeted therapeutic research, ranked by the number of indexed affiliation occurrences.

Rank	Affiliation	Documents
1	University of Texas MD Anderson Cancer Center	552
2	Memorial Sloan Kettering Cancer Center	421
3	Dana-Farber Cancer Institute	288
4	University of California San Francisco	219
5	Shanghai Jiao Tong University	200
6	Fudan University	199
7	Sun Yat-sen University	190
8	Harvard Medical School	187
9	Zhejiang University	149
10	Genentech Inc.	142

Table 3
c. Most frequent indexed author strings in KRAS-targeted therapeutic research. Values represent name-string frequencies and should not be interpreted as disambiguated individual-author counts.

Rank	Author string	Documents
1	Wang Y	161
2	Zhang Y	150
3	Wang J	96
4	Liu Y	95
5	Li Y	94
6	Zhang J	94
7	Wang X	88
8	Wang	78
9	Li J	75
10	Wang Z	67

Keyword co-occurrence and trend-topic structure

The keyword co-occurrence network was organized around a central KRAS/cancer vocabulary, with closely connected terms related to mutation, activation, resistance, inhibition, RAS protein, cancer, lung cancer, colorectal cancer, and molecular targeted therapy (Fig. 6).

Trend-topic analysis showed an early phase characterized by gene therapy, farnesyltransferase inhibitors, EGFR, signal-regulated kinase, synthetic lethal interaction, mouse models, and antitumor activity. From the late 2010s onward, the literature increasingly emphasized KRAS, lung cancer, colorectal cancer, mutation, pathway activation, therapy, and RAS protein. Recent hotspots shifted toward non-small-cell lung cancer, colorectal cancer, efficacy, and molecular targeted therapy, indicating a movement from indirect targeting and pathway biology toward allele-specific precision oncology (Fig. 7).

Collaboration and intellectual structure

The collaboration network showed multiple author communities with dense within-cluster links and cross-cluster connections, indicating that KRAS-targeted therapy research is collaborative but not organized around a single centralized author group (Fig. 8).

The author co-citation network identified three major clusters, reflecting distinct but interconnected schools of thought within the KRAS-targeted therapy literature (Fig. 9). The largest cluster was centered on Skoulidis, Hallin, Awad, and Ryan, while the remaining clusters were dominated by Cox and colleagues and Janes, Prior, and colleagues.

Most globally cited documents and pivotal studies

The most globally cited documents reflected both early KRAS pathway biology and later clinical translation of direct mutant KRAS inhibition (Table 4). Barbie et al. was the most globally cited document, reflecting the early influence of synthetic-vulnerability approaches in KRAS-driven cancers. Engelman et al. (2008) also represented pathway-based therapeutic work rather than direct KRAS inhibition, which is important when interpreting the table as KRAS-targeted therapeutic research rather than only modern direct-inhibitor research.

Ostrem et al. (2013), Janes et al. (2018), Canon et al. (2019), and Hallin et al. (2020) anchored the chemical-biology and preclinical development of direct KRAS G12C inhibition. Hong et al. (2020), Skoulidis et al. (2021), Jänne et al. (2022), and de Langen et al. (2023) reflect clinical translation of KRAS G12C inhibitors in advanced solid tumors and NSCLC. Awad et al. (2021) highlighted acquired resistance to KRAS G12C inhibition, supporting the bibliometric signal that resistance and combination strategies remain major ongoing themes.

Table 4
Most globally cited documents in KRAS-targeted therapeutic research, ranked by total citations.

Rank	Document	DOI	Total citations	TC per year
1	Barbie DA, 2009, Nature	10.1038/nature08460	3,036	168.7
2	Ostrem JM, 2013, Nature	10.1038/nature12796	2,070	147.9
3	Skoulidis F, 2021, New England Journal of Medicine	10.1056/NEJMoa2103695	1,477	246.2
4	Canon J, 2019, Nature	10.1038/s41586-019-1694-1	1,433	179.1
5	Hong DS, 2020, New England Journal of Medicine	10.1056/NEJMoa1917239	1,415	202.1
6	Skoulidis F, 2018, Cancer Discovery	10.1158/2159-8290.CD-18-0099	1,370	152.2
7	Engelman JA, 2008, Nature Medicine	10.1038/nm.1890	1,155	60.8
8	Hallin J, 2020, Cancer Discovery	10.1158/2159-8290.CD-19-1167	975	139.3
9	Awad MM, 2021, New England Journal of Medicine	10.1056/NEJMoa2105281	948	158.0
10	Janes MR, 2018, Cell	10.1016/j.cell.2018.01.006	940	104.4

Discussion

The KRAS-targeted therapy literature has grown into a substantial body of work, with 3,265 articles and reviews indexed between 2006 and 2026 and a clear upward inflection in output after 2020. This trajectory reflects the maturation of a genuine research field rather than a change in indexing practice. The most informative feature of this trajectory is its timing rather than its rate of growth, as the acceleration coincides with the clinical emergence of direct mutant KRAS inhibition and a corresponding reorganization of the field's thematic structure (Hong et al., 2020, Skoulidis et al., 2021). Because bibliometric growth is an observational signal, it indicates when and where research activity became concentrated rather than establishing that any single drug or trial caused this increase, a limitation that applies throughout the present analysis.

From indirect targeting to direct KRAS inhibition

The trend-topic and co-occurrence results trace a coherent intellectual history. Early vocabulary centered on farnesyltransferase inhibition, downstream kinase signaling, synthetic lethal interactions, and murine tumor models, terms that describe attempts to establish whether KRAS-driven cancers could be controlled at all while the oncoprotein itself resisted direct engagement (Figs. 6&7). The later vocabulary

is qualitatively different. Allele-specific labels such as KRAS G12C, individual drug names, and outcome-oriented terms including efficacy and molecular targeted therapy point to a literature organized around agents that act on mutant KRAS directly and are assessed within defined clinical categories. Rather than reflecting a change in the underlying scientific problem, this shift indicates that direct mutant KRAS inhibition had become a realistic therapeutic objective (Figs. 6&7).

The most globally cited documents mirror this evolution of the field. Ostrem et al. (2013) supplied the chemical foundation by showing that the switch-II pocket of KRAS G12C could be engaged covalently, and Janes et al. and Canon et al. carried that insight into therapeutic development. The clinical studies of sotorasib and adagrasib by Hong et al. (2020), Skoulidis et al. (2021), Jänne et al. (2022), and de Langen et al. (2023) subsequently established activity in advanced solid tumors and NSCLC, the point at which annual output began to rise steeply. Two of the highest-cited works sit outside this direct-inhibition lineage, since Barbie et al. (2009), the single most cited document, identified a synthetic vulnerability in KRAS-driven cancers, and Engelman et al. (2008) examined combined pathway inhibition in KRAS-mutant models. Their prominence indicates that the intellectual base of the field still rests partly on the pathway biology that preceded direct inhibitors, so a citation ranking of KRAS-targeted research captures this broader lineage rather than modern inhibitors alone. The concentration of these landmark studies within a small number of research environments is also visible in the geographic and institutional structure of the wider literature.

Geographic, institutional, and collaborative structure

Country-level results place the United States and China at the front of the field, although the two lead on different measures; China's affiliation frequency rose steeply in the most recent years, whereas the United States retained the highest citation impact across the study period. Read together, this divergence may be attributed to the difference between recent participation and accumulated influence rather than a single ranking of national output. Part of the gap is structural, because citations favor older works (Chow et al., 2023), including much of China's recent contribution, which have had less time to accrue them. Country values here also represent affiliation of occurrence rather than unique publications, so they index involvement in the indexed literature rather than a precise measure of national research volume.

Institutional and collaborative patterns are consistent with the kind of research the field demands. The most active affiliations were comprehensive cancer centers and translational programs with industry links, environments that can integrate medicinal chemistry with molecular oncology and early-phase clinical development in one setting. Rather than concentrating around a single dominant group, the co-authorship network resolved into several overlapping communities, and the author co-citation structure separated into recognizable clusters spanning foundational drugability and chemical biology, clinical KRAS G12C translation, and RAS pathway and resistance biology. These clusters suggest that progress has occurred through multiple complementary research programs rather than a single dominant investigative lineage. The author-string results warrant more caution, since abbreviated names can merge distinct individuals and were reported as indexed name-string frequencies rather than

disambiguated author counts. Where these communities now direct their attention indicates the questions likely to define the next phase of the field.

The emergence of KRAS G12D alongside broader molecular targeted therapy terms in the most recent keyword data suggests that the field is already progressing beyond its initial objective and extending its focus beyond the G12C allele that defined the first wave of direct inhibitors. The emergence of broader concepts such as pan-KRAS and RAS(ON) inhibition within the recent literature further supports this diversification of therapeutic strategies (Feng et al., 2025) (Holderfield et al., 2024). Set against the sustained influence of Awad et al. (Awad et al., 2021) and the persistence of resistance-related terms, this pattern points to a reframing of the central question, from whether mutant KRAS can be inhibited to whether inhibition can be broadened across alleles and sustained against adaptive escape. These themes remain early, and their prominence in the trend analysis reflects concentrated recent interest rather than a settled clinical direction.

Such signals indicate where progress will most likely be contested rather than what its outcome will be. Whether this momentum translates into durable clinical benefit will depend largely on the field's ability to overcome resistance while broadening effective targeting beyond KRAS G12C. Bibliometric analysis cannot speak to whether these efforts will succeed. It identifies where scientific attention and citation activity are gathering, and the value of the present mapping lies in making that concentration explicit rather than in anticipating clinical results.

Limitations

Several limitations should be considered. First, as a keyword-based topic search, the strategy cannot fully separate studies targeting KRAS from those in which KRAS status serves as a predictive biomarker for other agents, most notably anti-EGFR therapy in colorectal cancer. This is visible in the citation record, where several publications reflect pathway-based or synthetic-lethal biology rather than direct inhibition. These records were considered within the intended scope of the analysis, which sought to capture the broader evolution of KRAS-targeted therapy, including its indirect and pathway-based origins, rather than direct inhibitors alone. This broader scope likely enriches the earlier and colorectal-associated literature, primarily influencing thematic composition rather than the overall growth trajectory or the emergence of G12C-related research. The analysis was restricted to the Web of Science Core Collection, selected for its standardized citation metadata and compatibility with established bibliometric software, although publications indexed exclusively in other databases may have been missed.

Beyond the search strategy, several factors may influence the interpretation of bibliometric metrics. Country and institutional counts are sensitive to multi-affiliation records, indexing conventions, and institutional naming variation, which is why country output is reported as country-affiliation occurrence frequency rather than unique publication counts; author-level results are likewise constrained by name ambiguity, particularly for common strings such as Wang Y or Zhang Y. Citation counts also favor older publications, meaning that more recent work, particularly from 2025 and 2026, where indexing may still

be incomplete, is likely to be underrepresented. Finally, these findings describe the evolution of the research landscape rather than the strength of the underlying evidence and should not be interpreted as measures of methodological quality or therapeutic efficacy.

Conclusion

This bibliometric analysis characterizes the development of KRAS-inhibitor therapy research in cancer between 2006 and 2026. Publication output increased steadily through the 2010s before accelerating sharply after 2020, paralleling the clinical translation of direct KRAS G12C inhibitors. Over this period, research evolved from indirect and pathway-based strategies, including farnesyltransferase inhibition and synthetic-lethal approaches, toward direct mutant KRAS inhibition and the clinical development of allele-specific therapies. Emerging keyword and trend analyses further suggest a growing emphasis on resistance mechanisms and non-G12C variants, particularly KRAS G12D, though these themes remain early and are best interpreted as indicators of research direction rather than established clinical fronts.

Research activity is concentrated in the USA and China, while the USA continues to have the greatest citation impact, with major contributions arising from leading translational cancer centers. Overall, the field has consolidated into a rapidly expanding area of precision oncology, with future progress likely to depend on overcoming therapeutic resistance and extending effective targeting beyond KRAS G12C to additional alleles and broader RAS-directed strategies. These findings describe patterns of scientific productivity, collaboration, and citation influence; they do not measure therapeutic efficacy or methodological quality and should be interpreted accordingly.

Abbreviations

KRAS, Kirsten rat sarcoma viral oncogene homolog; TC, total citations; WoSCC, Web of Science Core Collection.

Declarations

Funding

No funding was received for this study.

Competing interests

The authors declare no competing interests.

Author contributions

AA, ZY, and JY conceived the study. AA performed the literature search, data curation, bibliometric analyses, and drafted the manuscript. ZY contributed to the methodology, data validation, and

manuscript revision. JY provided methodological guidance and critically revised the manuscript. All authors approved the final manuscript.

Data availability

The bibliographic dataset analyzed during the current study is available from the corresponding author on reasonable request, subject to Web of Science licensing restrictions.

Ethics approval

Not applicable. This bibliometric analysis used publicly indexed bibliographic metadata and did not involve human participants, human data, animals, or biological material.

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Figures

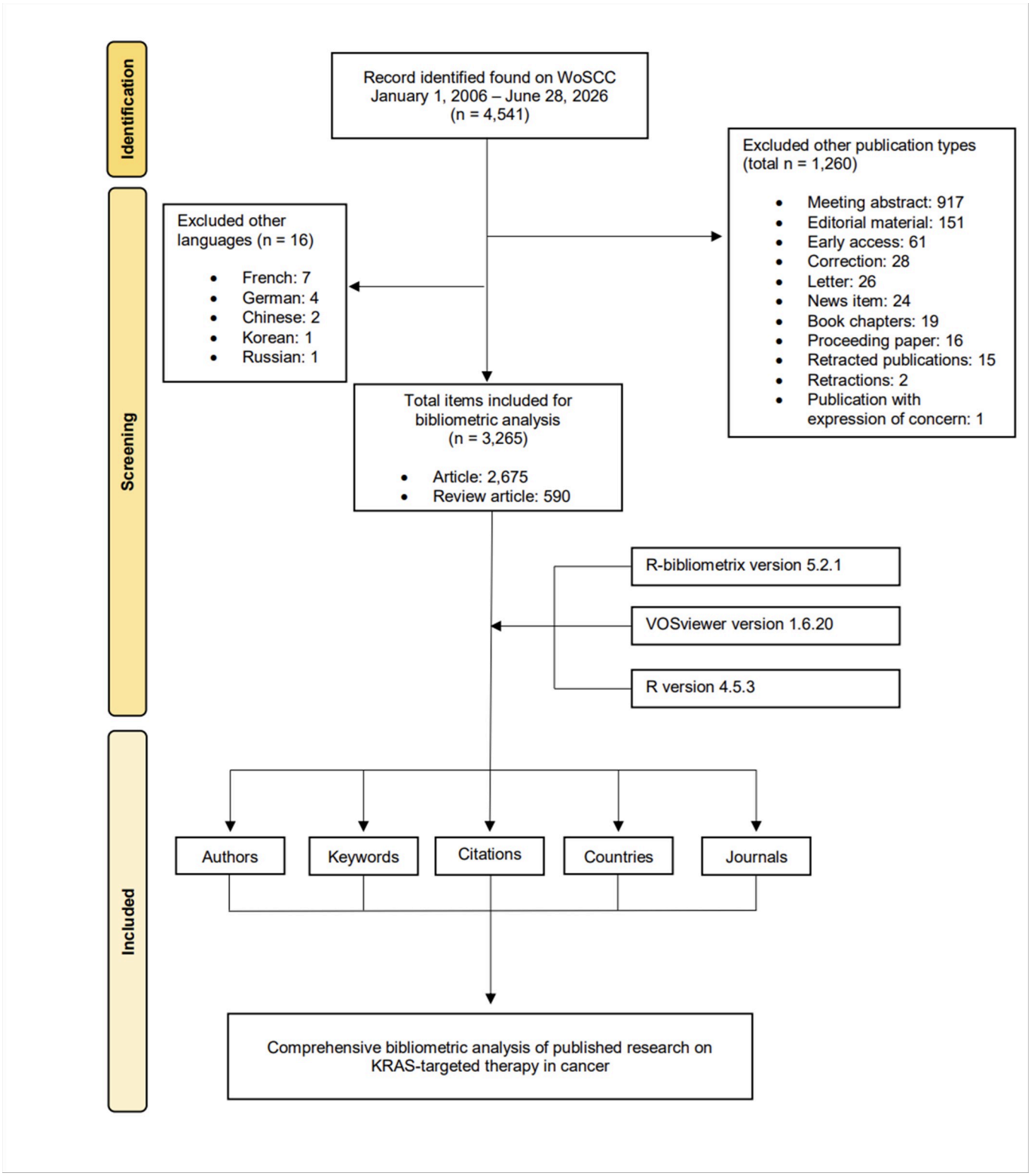


Figure 1

Study selection flow diagram. Flow diagram summarizing identification of Web of Science Core Collection records, restriction to eligible document types, and final inclusion in the bibliometric analysis.

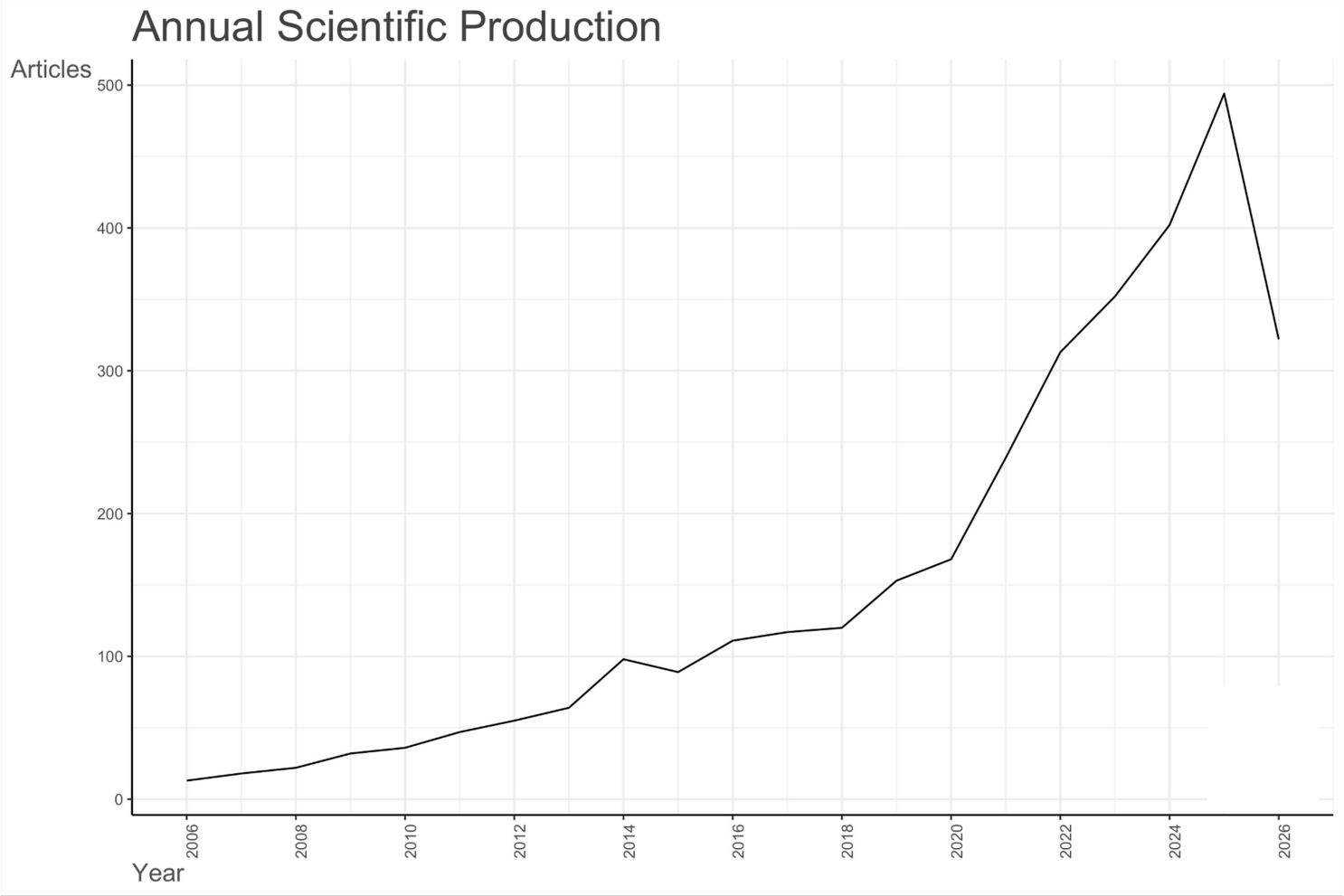


Figure 2

Annual scientific production in KRAS-targeted therapy research from 2006 to 2026. The line shows the number of included articles and reviews indexed by publication year.

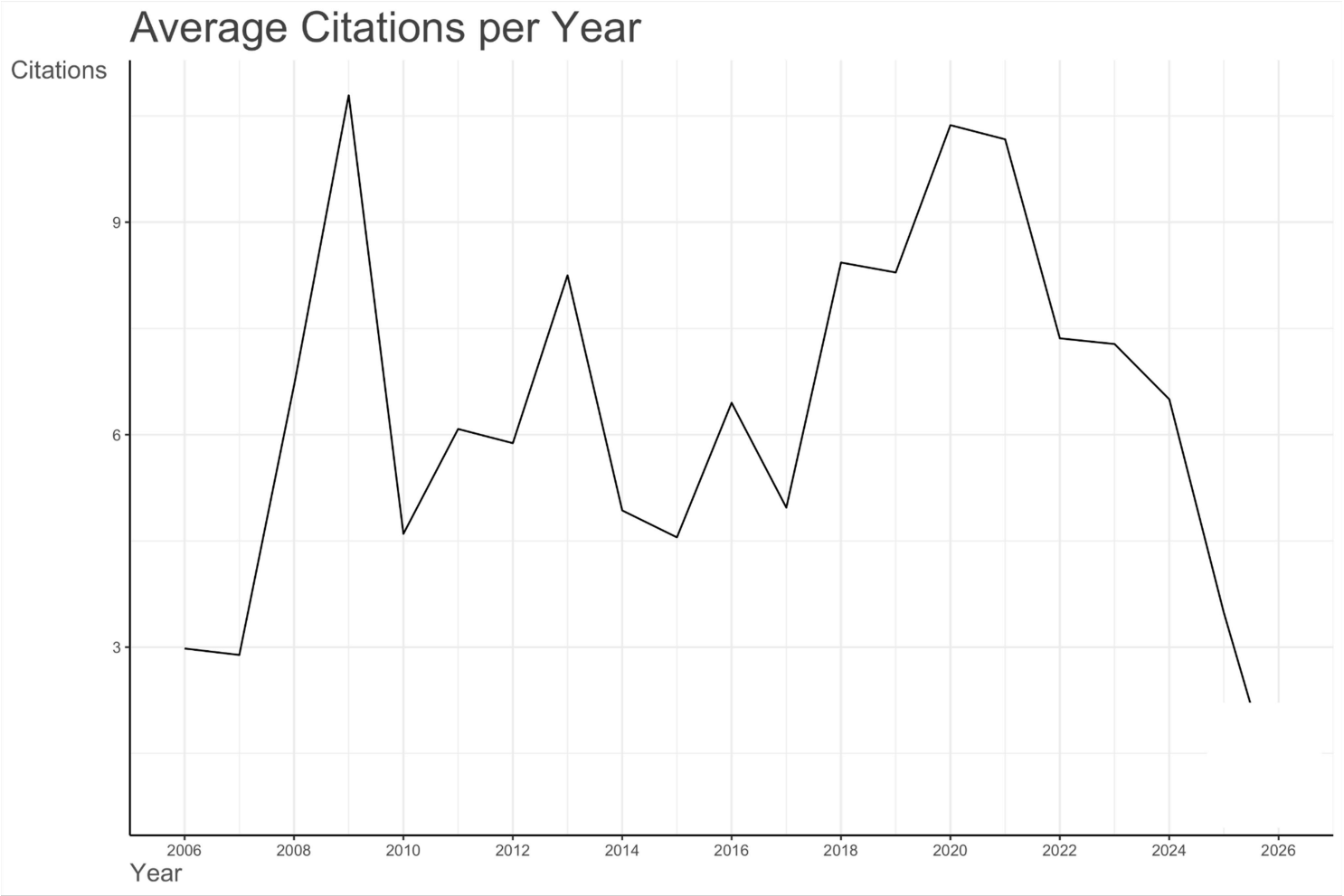


Figure 3

Average article citations per year. The line shows the average annual citation rate by publication year; recent years should be interpreted in the context of citation lag

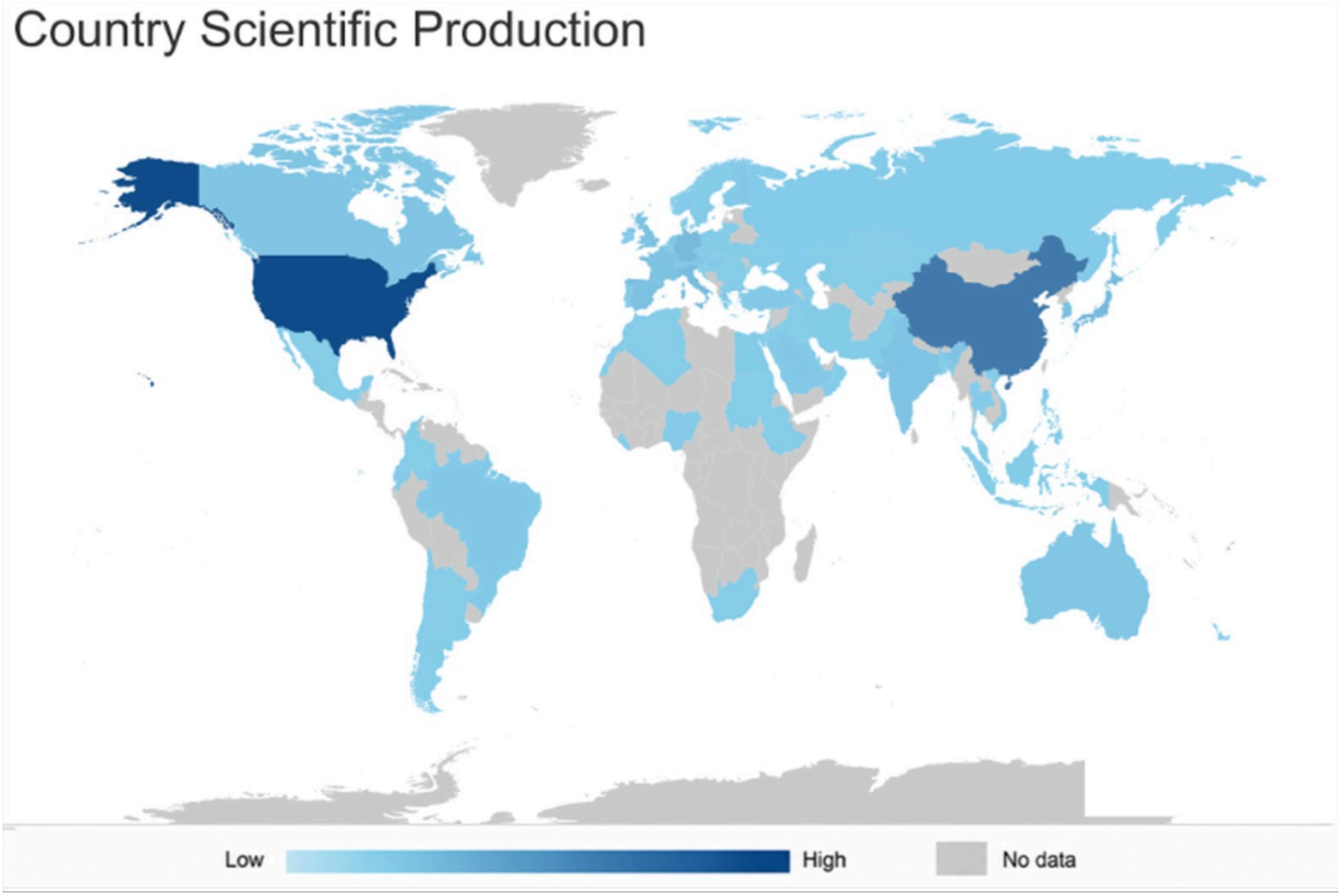


Figure 4

Country scientific production map for KRAS-targeted therapy research. Darker shading indicates higher country-affiliation occurrence frequency in the included records.

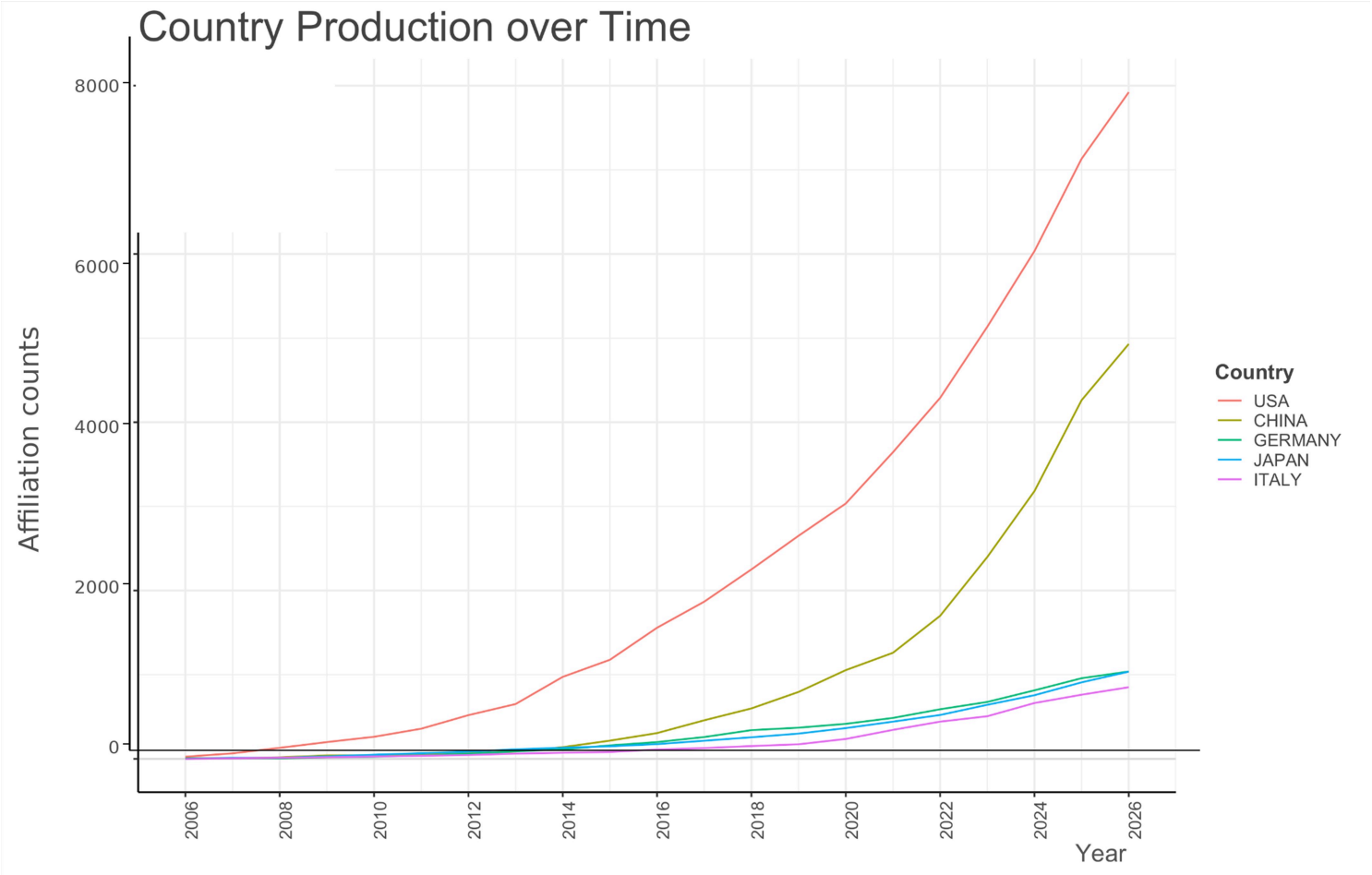


Figure 5

Country production over time for the five leading countries. The y-axis represents cumulative country-affiliation occurrence frequency rather than unique publication counts.

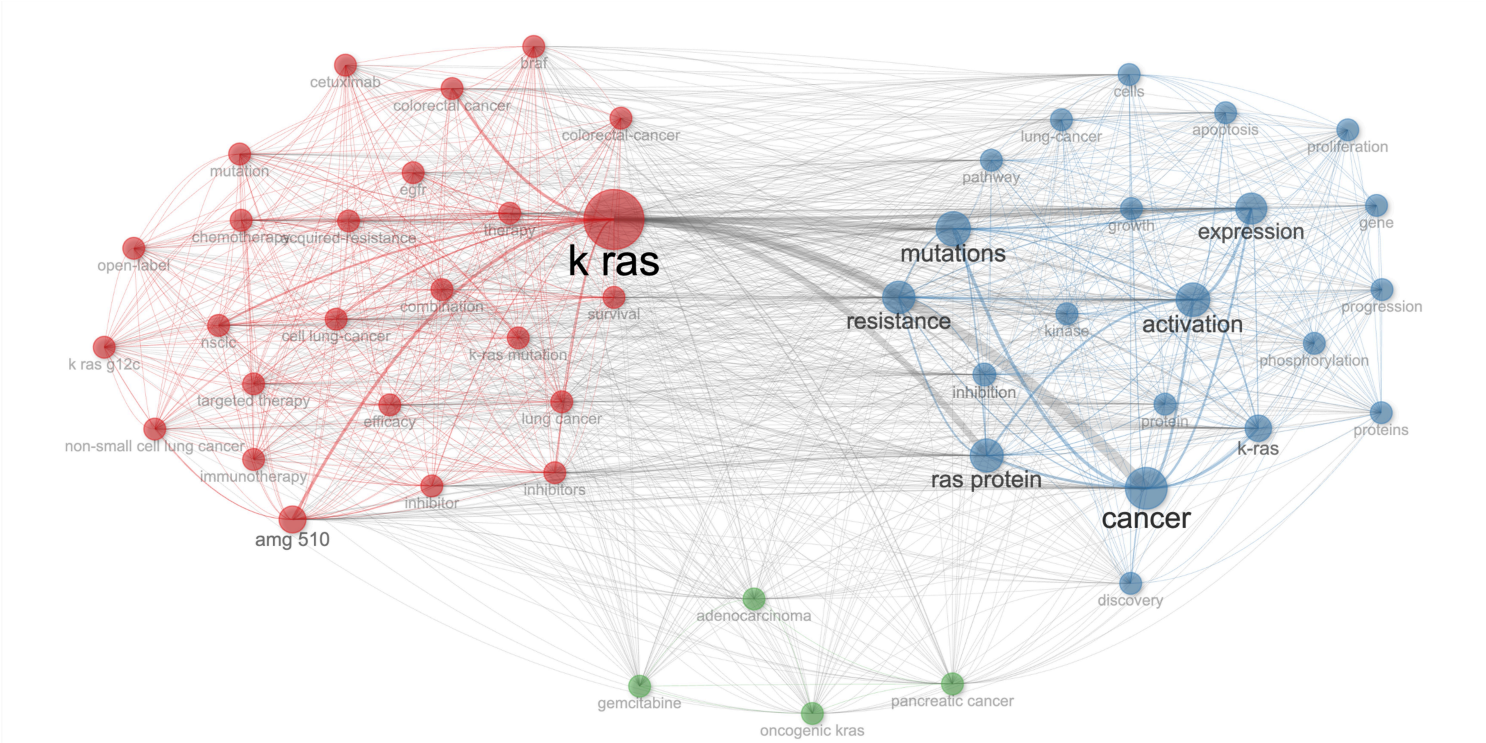


Figure 6

Keyword co-occurrence network in KRAS-targeted therapy research.

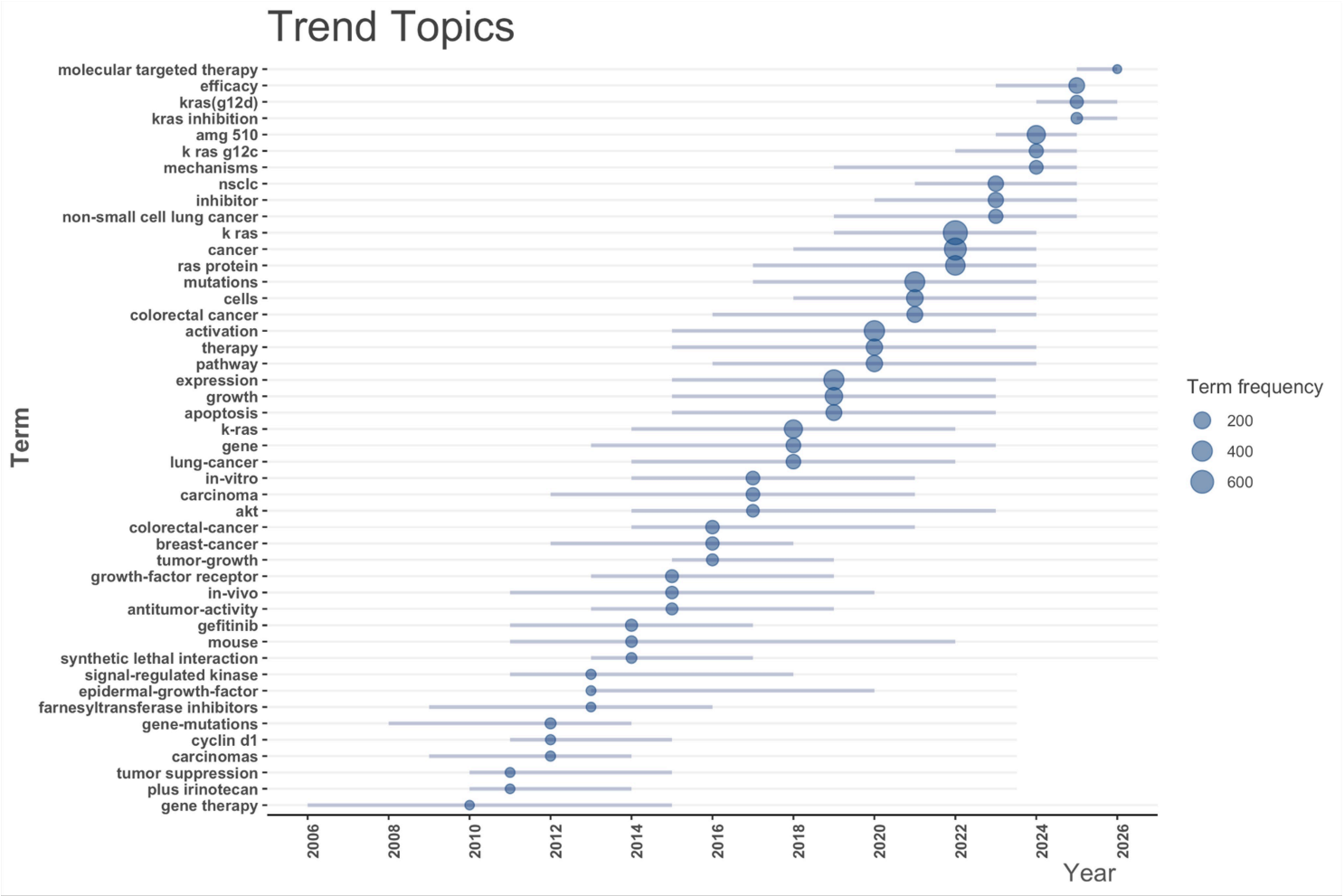


Figure 7

Trend-topic analysis of KRAS-targeted therapy research. Circle size reflects term frequency; horizontal lines indicate the period over which each term appeared, and circle position indicates the median year of use.

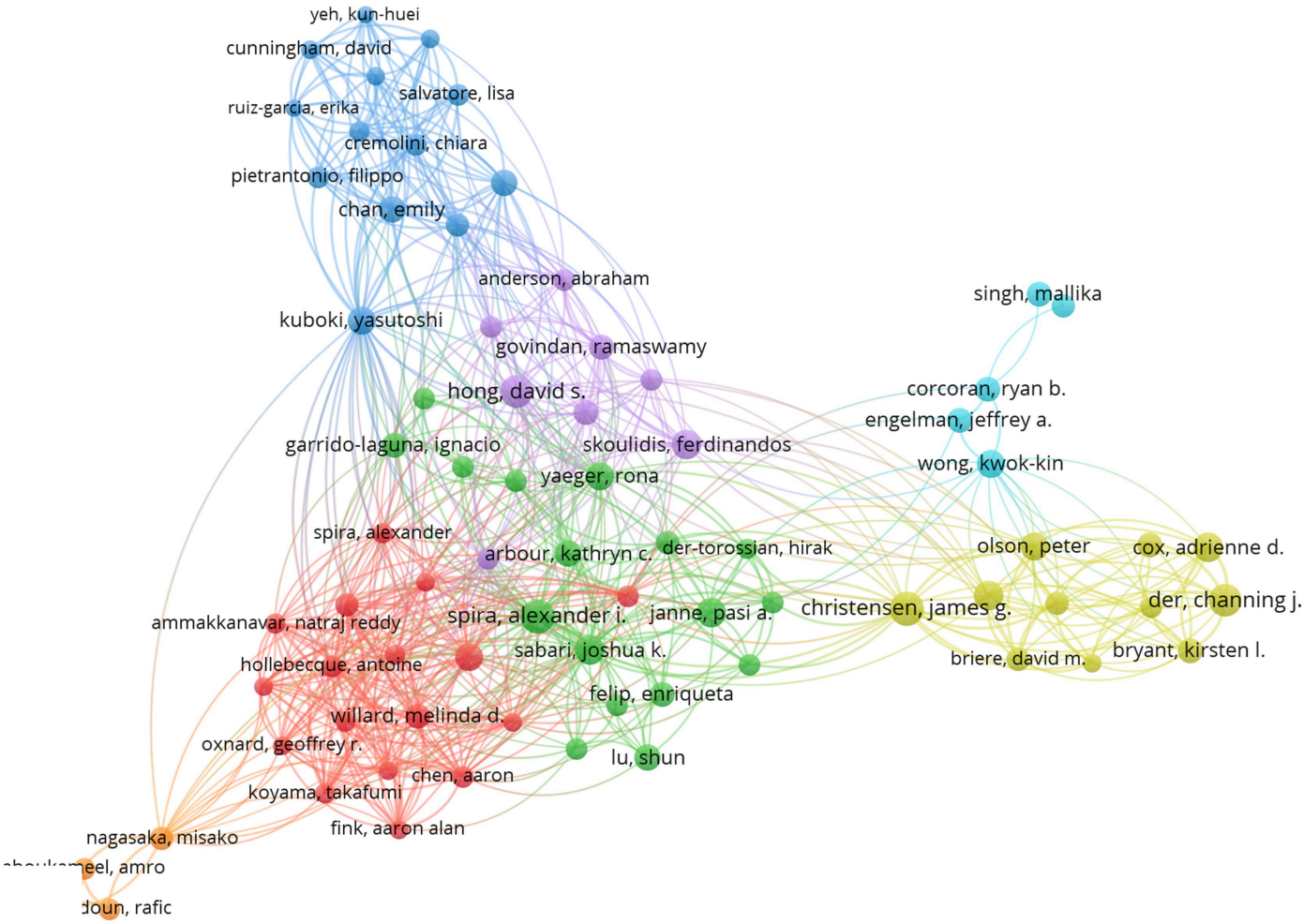


Figure 8

Author co-authorship network. Node size reflects author weight within the collaboration network, links indicate co-authorship relationships, and colors represent author clusters.

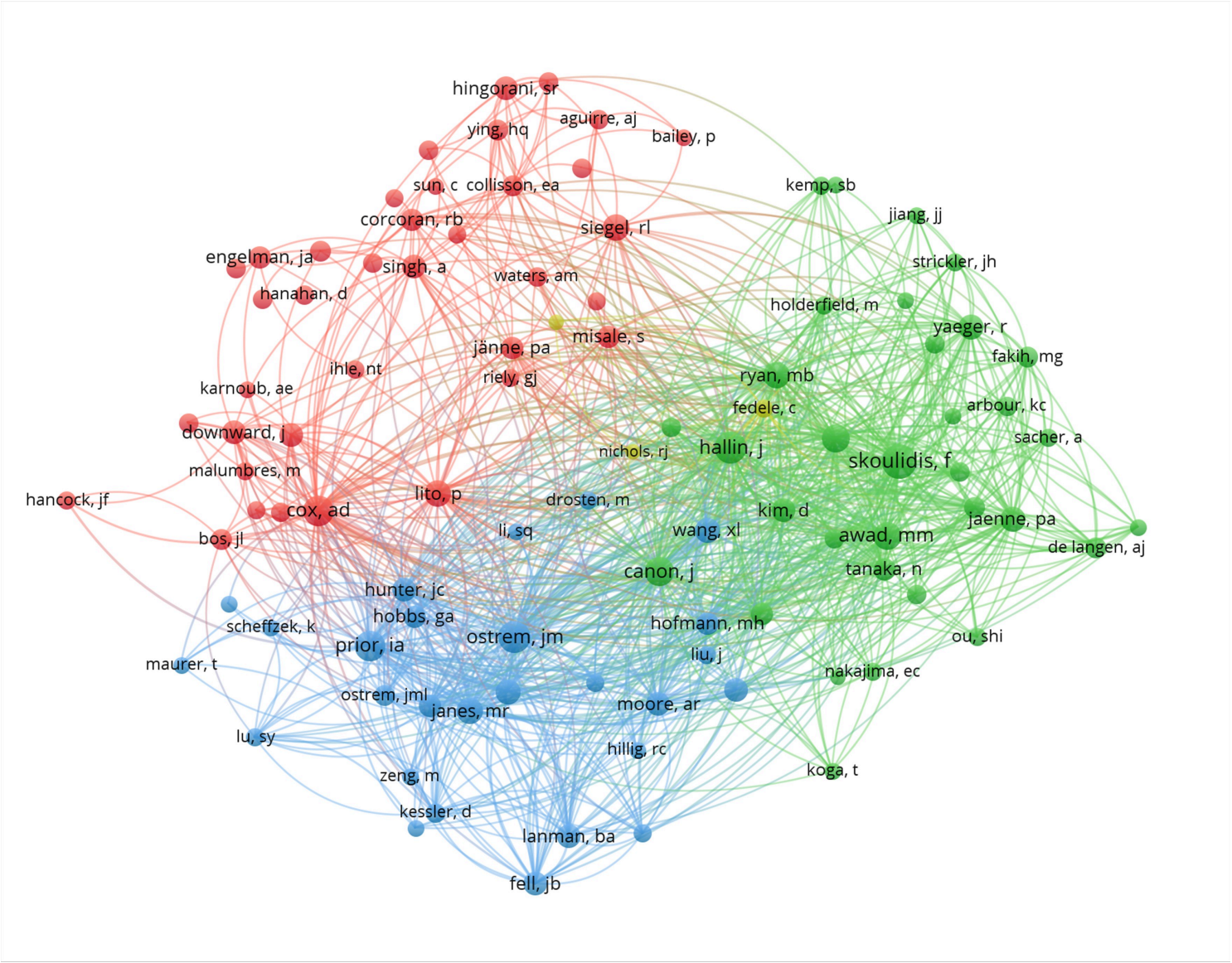


Figure 9

Author co-citation network. Node size reflects co-citation weight; links indicate co-citation relationships, and colors represent clusters of authors frequently cited together.