

# A Scientometric Analysis of Neuroblastoma Research

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## Research article

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# Abstract

**Background:** There are thousands of research articles in the field of neuroblastoma that have been published over the past few decades. However, the heterogeneity and variable quality of scholarly data may challenge scientists or clinicians to survey all published articles. However, holistic measuring and analyzing of neuroblastoma related literature by sophisticated mathematical methods can provide a unique opportunity to gain deep insights into the global research performance and collaborative architectural structure within the neuroblastoma scientific community. In this scientometric study, we aim to determine the extent of the scientific output related to neuroblastoma research, focusing on the time period between 1980 and 2018.

**Methods:** We apply novel scientometric tools, including Bibliometrix R package, biblioshiny, VOSviewer, and CiteSpace IV for comprehensive science mapping analysis of extensive bibliographic metadata which was retrieved from the Web of Science™ Core Collection database.

**Results:** We demonstrate the enormous proliferation of neuroblastoma research during last the 38 years, including 12,435 documents published in 1,828 academic journals by 36,908 authors from 86 different countries. We determine the proportion of highly cited and never cited papers, “occasional” and “core” authors and journals. We identify the six most important clusters of authors and their interactions. Further, we show 10 (11.6%) of 86 countries were responsible for the three quarters of NB-related research output.

**Conclusions:** These findings are crucial for researchers, clinicians, journal editors, and consortiums working in neuroblastoma area to understand the strengths and potential gaps in neuroblastoma research and to plan future investments in data collection and science policy. This first scientometric study of global neuroblastoma research performance provides valuable insight into the scientific landscape, co-authorship network architecture, international collaboration, and interaction within the neuroblastoma community.

## Background

Neuroblastoma (NB) is the most extracranial malignant pediatric tumor that typically arises in the adrenal medulla or paraspinal sympathetic ganglia. (1) The histological differentiation state of NB is highly variable, including undifferentiated “small blue round cell” neoplasms, partial differentiated ganglioneuroblastomas (GNB), and differentiated ganglioneuroma (GN), which consists of clusters of mature neurons surrounded by a dense stroma of Schwann cells. As an immature tumor, NB is aggressive, predominantly occurring in early childhood at a median age of 22 months and accounting for 15% of childhood cancer-related mortality. The overall survival rate for high-risk metastatic diseases is 40%. (2–5) Conversely, mature variants (GNB or GN) occur in older children and tend to behave in a more benign fashion. (6)

In addition to tumor histology, many molecular genetic markers of NB have been identified, including: amplification of the N-myc proto-oncogene protein (MYCN), mutations of the anaplastic lymphoma kinase (ALK) receptor, allelic deletions in the 1p, 3p and 11q chromosomal regions, chromosomal gain of 17 or tumor cell ploidy. (7,8) Amplification of the MYCN gene is associated with poor prognosis and was found in about 20% of NB cases. (9,10) ALK is altered by gain-of-function point mutations in around 14% of high-risk NB and confers poorer prognosis for tumors in the intermediate- and high-risk categories. (11,12)

Treatment regimens for patients with NB differ accordingly and depend on tumor behavior as predicted by tumor histology and molecular features. (13) Children with low-risk NB can be observed or treated surgically while those with intermediate risk disease may receive chemotherapy prior to surgical resection. Patients with high-risk NB undergo intensive multimodal therapy including chemotherapy, surgical treatment, stem cell transplantation, radiation, and immunotherapy. (14,15)

Over the past decades, national and international collaborative research efforts have led to increased knowledge of biological and clinical tumor features, thereby refining patient's risk stratification and treatment strategies, leading to significant increases in survival rates. Currently, patients with low- and intermediate-risk NB have an overall survival rate of about 90%. (16,17) However, children with high-risk NB still have a poor prognosis. (3) To improve understanding of the genetic basis of NB, the neuroblastoma research community has collected large numbers of tumor and germline samples. With this, key somatic and germline genomic alterations have been discovered. These collective advancements have led to the development of new therapeutic approaches for high-risk NB. (18)

Given the enormous volume, heterogeneity and variable quality of NB-related publications, an assessment of the scientific literature on this topic is essential for both clinicians and researchers. Hence, we employed scientometric methodologies and innovative visualization tools to extract extensive bibliographic metadata related to NB research. We performed an analysis of co-authorship network architecture, which provides valuable insight into the topography of the NB community. In this study, we report on scientific NB publications produced between 1980 and 2018.

## Methods

All peer-reviewed scientific publications relating to NB research were retrieved from the Web of Science™ Core Collection Database (Clarivate Analysis, Boston, USA). The search terms {"neuroblastoma(s)"} OR {"ganglioneuroblastoma(s)"} OR {"ganglioneuroma(s)"} OR {"peripheral neuroblastic tumor(s)"} were used in the title field and results were filtered by publication year from 1980 through 2018. No language restrictions were imposed. The complete metadata for each original publication and review article was compiled and manually exported on November 12, 2019. The "citation report" function was applied to assess citation rates and h-index.

Bibliometrix (version 1.7), an R-Tool of R-Studio (Version 3.6.1) for comprehensive science mapping analysis, and biblioshiny, the shiny interface providing a web-interface for bibliometrix, were used to

import and manage the metadata from Web of Science™. (19) Baseline metadata included print features, such as author's name, corresponding author's country (CAC), total number of publications, single country publication (SCP), multiple countries publications (MCP), citations count with total citations (TC), average article citations (AAC), number of citing articles with and without self-citations, journal sources, keywords, countries/regions, and the author-level metrics such as h-, m-, and g indices. The h-index, a common proxy measure for individual scientific output, is defined as the number of papers with citation number  $\geq h$  (at least one citation). (20) Consequently, the h-index depends on both the number of a scientist's publications and their impact on peers (number of citations). Since the h-index does not account for the career span of the author, the m-index or m-quotient (equal to the h-index divided by the number of years since the author's first publication [m-quotient = h-index/n, n = number of years since the first published paper of the scientist]) was applied. Further, to account for the citation evolution of the most cited papers of the given author over time, the g-index, which gives credit for the most highly cited papers in a data set, was used.

Lotka's law was used to determine the scientific productivity of authors in the field of NB. Briefly, Lotka's law indicates that the number of researches making  $n$  contributions/publications during a certain time period is a fraction of the number of researchers making a single contribution, following the formula  $1 / n^a$  where  $a$  nearly always equals two. (21) The number of authors publishing a certain number of papers is a fixed ratio ( $B = 2$ ) to the number of authors publishing a single paper. (22) The deviation of the observed function from the predicted inverse square function acts as a metric for the inequality in productivity of the field. (23) Additionally, "core" authors with at least two publications related to NB and "occasional" authors with only a single NB article were identified. Source clustering was carried out through Bradford's law. (24)

Bradford's law describes the distribution of the scientific articles related to a specific topic in journals that are not specifically dedicated to this topic itself. Consequently, we could group journals within "core zones", comprised those particularly devoted to the NB subject.

Collaboration measures include the number of documents per author (documents/author), number of authors per document (author/document), co-authors per document (authors appearance/documents), and collaboration index (CI). CI was calculated for the entire dataset and each cluster as a ratio of the number of authors of coauthored articles to the total number of co-authored articles. (25)

In addition, using the word co-occurrence in our bibliographic data collection. we mapped the conceptual structure of an entire word's framework with a dimensionality reduction technique and Multiple Correspondence Analysis (MCA) (26) We identified clusters of documents which express common concepts. Words appearing together in an article were related in a network.

VOSviewer (version 1.6.13, <http://www.vosviewer.com>), a network analysis software tool, was used to construct a collaboration network based on co-authorship and keyword co-occurrence. (27) We utilized fractional counting and excluded publications with more than 10 co-authors in order to prevent biasing of

the network structure according to Perianes-Rodriguez et al. (28) The size of the circles in the VOSviewer diagram indicate the number of publications per author, the colors indicate clusters, the lines collaborations, and the thickness represents the strength of collaborations. The link strength between the circles refers to the frequency of author's co-occurrence. The total link strength is the sum of link strengths of the author (circle) over all the other authors.

CiteSpace IV (Drexel University, Philadelphia, PA, USA, Version 0.65) was applied to determine the keywords with strong citation bursts, which serves as an indicator of the most active area of research attracting a special degree of attention from the scientific community. Relationships between author's keywords, references used, and the top authors were summarized by a Sankey plot (three-fields plot).

Categorical variables were expressed as frequency and percentage, continuous variables were represented as medians with maximum and minimum or as means with standard deviation. The Spearman correlation coefficient was used to test correlations between selected continuous variables. Statistical analyses were performed with SPSS v. 23 (SPSS 23.0 – SPSS Inc, Chicago Illinois) and GraphPad Prism v. 6.01 (GraphPad, La Jolla, CA). All tests were two-sided. P-values of < 0.05 were considered statistically significant. This study did not require approval of an ethic committee.

## Results

### Overall publication performance and dynamics

We first assessed the overall publication performance in neuroblastoma research during the last 38 years. In total, 12,435 documents, including 11,970 (96.2%) articles and 465 (9.8%) reviews, were published by 36,908 authors from 86 countries. The annual percentage growth rate indicating increasing annual scientific production was 11.8%. Linear fitting of the data revealed an increase in the number of publications written between 1980 and 2018 ( $r^2 = 0.92$  [CI: 0.86 to 0.96];  $p < 0.0001$ ). Of 12,136 retrieved documents, a total of 316,017 received citations including self-citations and 289,357 were without self-citations. The average citation per document was  $28.35 \pm 7.7$ . There was a consistent citation dynamic ranging from 29.5 CPI in 1980 to 30.8 CPI in 2010. After 2011, the CPI was 12.7, which was lower compared to period the 1980–2010, because most newly published articles had not been cited much at the time of data extraction in our study. While the number of single-authored documents remains stable over the time ( $r^2 = -0.6$ ,  $p = 0.24$ ), the number of multi-authored documents increased significantly ( $r^2 = 1.0$ ,  $p = 0.003$ ) (Fig. 1, Table S1). The overall collaboration index (CI) was 3.02. The majority of papers were published by authors in the United States ( $n = 3,202$ , 25.7%), Japan ( $n = 1,222$ , 9.8%), Italy ( $n = 1,129$ , 9.1%), Germany ( $n = 824$ , 6.6%), China ( $n = 741$ , 5.9%), the United Kingdom ( $n = 688$ , 5.5%) and France ( $n = 538$ , 4.3%). Among 1,828 journals represented in our dataset, the five most productive were Journal of Neurochemistry ( $n = 319$ , 17.4%), Cancer Research ( $n = 295$ , 16.1%), Journal of Pediatric Surgery ( $n = 278$ , 15.2%), Pediatric Blood and Cancer ( $n = 261$ , 14.3%), and Medical and Pediatric Oncology ( $n = 225$ , 12.3%).

# Profiling of authors

In the entire dataset of 36,908 authors, 25,873 authors (70.1%) published a single paper related to neuroblastoma and were considered “occasional” authors; 5,178 (14.0%) published two papers; 2,076 (5.6%) published three papers; 3,781 (10.2%) published four or more papers. Authors who published more than one paper were considered to be “core” authors. The Lotka’s law estimation yielded a beta coefficient ( $\beta$ ) of 2.3 and a constant coefficient (c) of 0.32 ( $r^2 = 0.92$ ). The Kolmogorov-Smirnov goodness-of-fit test found Lotka’s law estimation to be insignificantly different from the theoretically predicted inverse square function ( $p = 0.89$ ). Additionally, the distribution of the number of publications per author had a hyperbolic aspect, according to Lotka’s law. This indicates that the author’s number of publications can be theoretically predicted and the research field of NB corresponds with the expected number of highly productive authors in the dataset according to Lotka’s law. Of the top 10 contributing authors, Berthold F was ranked first in the number of published articles ( $n = 169$ ), Matthay KK had the highest h- and m-indices (63 and 2.2, respectively) while Seeger RC had the highest average citation per item count (100.2) (Table 1). Scientific productivity of the top authors on neuroblastoma research over time is presented in Figure S1.

Table 1  
Top 10 contributing authors in field of neuroblastoma research

Source	IF	NP	TC	h-index	g-index	m-index
Journal of Neurochemistry	4.87	319	10221	53	71	1.39
Cancer Research	9.13	295	19170	80	117	2.35
Journal of Pediatric Surgery	2.09	278	4409	33	45	0.86
Pediatric Blood and Cancer	2.64	261	3368	27	40	1.68
Oncogene	6.85	194	9223	55	82	1.83
PLOS One	2.77	193	3528	27	43	2.07
Neuroscience Letters	2.15	192	3568	31	45	0.86
Journal of Clinical Oncology	26.3	180	16426	75	121	2.20
European Journal of Cancer	7.19	178	5229	40	57	1.37
International Journal of Cancer	7.3	172	5123	35	74	1.22

The network analysis revealed six clusters of authors ( $n_1 = 10, n_2 = 10, n_3 = 6, n_4 = 4, n_5 = 4, n_6 = 3$ ). (Fig. 2, Table S2). To examine collective performance, the total number of publications, mean h-indices, and average citations per item of the authors in each cluster were calculated using only articles in the dataset across all years. A Kruskal-Wallis test found significant differences between clusters according to h-indices ( $p = 0.02$ , post hoc Mann Whitney test: cluster 2 vs cluster 1,  $p = 0.001$ ) and average citations per

item ( $p = 0.001$ , post-hoc Mann Whitney test: cluster 2 vs cluster 1,  $p < 0.0001$ ; cluster 2 vs cluster 5,  $p = 0.008$ ) with dominance of cluster 2. There were no differences in total number of publications between the clusters. The CI for each group was calculated ( $CI_1 = 2.56$ ;  $CI_2 = 3.02$ ;  $CI_3 = 2.67$ ;  $CI_4 = 1.98$ ;  $CI_5 = 2.12$ ;  $CI_6 = 1.97$ ), indicating that group 2 was the most internally collaborative in the dataset.

## Source landscapes

In the time frame analyzed, there were 1,828 academic journals publishing papers related to neuroblastoma research. Journal of Neurochemistry (impact factor [IF] 2018 = 4.87) had the highest publication output ( $n = 319$ , 17.4%), followed by Cancer Research (IF 2018 = 8.37;  $n = 295$ , 16.1%), Journal of Pediatric Surgery (IF 2018 = 2.09;  $n = 278$ , 15.2%), and Pediatric Blood and Cancer (IF 2018 = 2.64;  $n = 261$ , 14.3%). The most cited journals were Cancer Research (19,170 citations), Journal of Biological Chemistry (16,699 citations), Journal of Clinical Oncology (14,403 articles), Proceedings of the National Academy of Sciences of the United States of America (12,602 articles), and Nature (11,440 articles). Table 2 summarized source impact of the top 10 journals publishing on neuroblastoma.

Table 2  
Source impact of the top 10 journals publishing on neuroblastoma

Region	TP	h-index	CAC	SCP	MCP (%)	TC	AAC
USA	4328	141	3202	2284	918 (21.2)	113525	35.45
Japan	1364	76	1222	1031	191 (14.0)	23268	24.66
Italy	1336	78	1129	864	265 (19.8)	26134	27.85
Germany	1128	85	824	580	244 (21.6)	21597	31.19
UK	910	75	688	467	221 (24.3)	18424	26.78
China	829	44	741	633	108 (13.0)	9144	32.61
France	748	70	538	371	167 (22.3)	14846	33.24
Sweden	454	56	355	219	136 (30.0)	10149	33.16
Spain	454	55	344	256	88 (19.4)	7610	30.00
Canada	427	52	289	199	90 (21.0)	7468	27.21

Source clustering through Bradford's law revealed that 23 (1.2%) journals published 4,168 (33.5%) of the articles on neuroblastoma as represented by the first zone (Figure S2). The middle zone, comprised of 157 (8.6%) journals, published 4,164 (33.4%) of the articles; the minor zone consists of 1,648 (90.2%) journals with 4,103 (33.1%) papers.

# Active countries and international collaborations

Eighty-six countries were involved in neuroblastoma total research output. Among them, 9,332 (75%) of publications were contributed by the top ten most productive countries (Table 3). The United States of America (USA) published the most papers (n = 4,328), had the highest h-index (141) and ranked first in terms of single country publications (n = 2,284). Researchers from the USA showed the highest collaboration performance with total link strength (TLS) of 1438, followed by Germany (TLS = 852), the United Kingdom (TLS = 829), Italy (TLS = 801), and France (TLS = 707). International collaboration (MCP) analysis showed that 136 articles (30.0%) produced by Sweden had international authors, followed by authors from the UK (n = 221, 24.3%), France (n = 167, 22.3%), Germany (n = 244, 21.6%), and the USA (n = 918, 21.2%).

Region	TP	<i>h</i> -index	CAC	SCP	MCP (%)	TC	AAC
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TP: total production; CAC: corresponding author's country; SCP: single country publication; MCP: multiple countries publications; TC: total citations; AAC: average article citations

Table 3

Most productive countries contributing to neuroblastoma research

The international collaboration network is presented in Figure S3. The number of links between any two countries represents the strength of collaboration, while the color intensity is proportional to the number of publications. The strongest collaboration was between the USA and Germany (frequency, n=160), the USA and Italy (n=156), the USA and the UK (n=137), and the UK and Italy (n=131).

# Most cited NB papers and NB papers without a single citation

Of 12,435 publications related to NB, 12,136 (94.8%) were cited at least one time and 299 (2.4%) publications remain uncited after their publication. Table 4 demonstrates the top 10 studies according to total number of citations. The review article entitled "Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment" published by Broder GM in Journal of Clinical Oncology in 1993 received the highest number of citations (n=1,450).

Author, year	Article	Journal	TC	TC per year
Broder GM, 1993 (29)	Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment.	J Clin Oncol	1,450	55.7
Kaghad M, 1997 (30)	Monoallelically expressed gene related to p53 at 1p36, a region frequently deleted in neuroblastoma and other human cancers	Cell	1,403	63.7
Broder GM, 2003 (7)	Neuroblastoma: Biological insights into a clinical enigma	Nat Rec Cancer	1,328	83.0
Matthay KK, 1999 (31)	Treatment of high-risk neuroblastoma with intensive chemotherapy, radiotherapy, autologous bone marrow transplantation, and 13-cis-retinoic acid	N Engl J Med	1,246	62.3
Maris JM, 2010 (32)	Neuroblastoma	Lancet	1,153	96.1
Maris JM, 2010 (3)	Recent Advances in Neuroblastoma	N Engl J Med	792	88.0
Yu A, 2010 (33)	Anti-GD2 Antibody with GM-CSF, Interleukin-2, and Isotretinoin for Neuroblastoma	N Engl J Med	707	78.5
Mosse YP, 2008 (34)	Identification of ALK as a major familial neuroblastoma predisposition gene	Nature	704	64.0
Shimada H, 1984 (35)	Histopathologic prognostic factors in neuroblastic tumors: definition of subtypes of ganglioneuroblastoma and an age-linked classification of neuroblastomas	J Natl Cancer Inst	686	19.6
Pule M, 2008 (36)	Virus-specific T cells engineered to coexpress tumor-specific receptors: persistence and antitumor activity in individuals with neuroblastoma	Nat Med	674	61.3

Table 4

Most cited neuroblastoma papers

## Keywords analysis

The most frequent author's keywords were "neuroblastoma" (n=4505), "apoptosis" (n=821), "differentiation" (n=371), "mycn" (n=262), "ganglioneuroma" (n=222), "oxidative stress" (n=218), "neuroblastoma cells" (n=214), "retinoic acid" (n=195), "chemotherapy" (n=153), "SH-SY5Y" (n=153). The overall keyword network visualization is presented in Figure 3. We identified keywords with a high-citation burst, which can be used to predict research areas attracting an extraordinary degree of attention from its scientific community (Figure S4). Next, we aimed to map the conceptual co-word structure using the word co-occurrences in our bibliographic metadata to identify clusters of documents which express common concepts. The results are plotted on a two-dimensional map (Figure S5). Overall, 7 clusters of words could be identified (each color represents a cluster of word). The three-fields plot shows the relationship between the author's keywords (research contents, right field), references authors use (intellectual roots, left field), and the top authors (middle field) (Figure S6).

## Discussion

In this scientometric study, we demonstrated the overall neuroblastoma research during the last 38 years, with the total number of publications reaching 12.435 articles in 2018 – an annual percentage growth rate of 11.8%. Overall, the number of NB related papers has increased 69-fold since the 1980s, probably reflecting the biological and clinical heterogeneity as well as the diversity of NB research sub-fields. (37) Moreover, intensive international collaboration research efforts are still ongoing as cure rates for the high-risk NB have shown only modest improvement. (38)

We found that 30% of 36.908 authors contributing to NB research were "core" authors, publishing two or more NB related articles. Correspondingly, the estimation of Lotka's law indicates similarity in author's productivity according to theoretically expectation. These findings mirror the results of the productivity analysis among 30 diverse scientific fields conducted by Ruiz-Castillo and Costas in 2014, revealing that 69% of authors have a single publication in the given field. (39)

We showed that 10 (11.6%) of 86 countries were responsible for three quarters of NB-related research output. Of these, the USA was the leading country regarding total number of publications, h-index, total citations, and average article citations. As a high-income country, the USA allocates a large budget for research and has a vast number of research centers. (40–42) Further, we demonstrated that the USA had

the highest collaboration performance, especially with Germany, Italy, and the UK, which additionally augments the research performance.

There is a global trend in science towards national and international collaborations to improve patient care. (43–45) Especially for NB as a rare and highly complex oncological disease, international collaboration is essential to conduct clinical trials of high statistical power by pooling data. Our network analysis yielded six clusters based on co-authorship patterns. These six co-authorship clusters differ in their size, activity and level of collaboration. The most internal collaborative and the most productive Cluster 2 consisted of ten researchers, including Reynolds CP, Seeger RC, Park JR, Matthay KK, Maris JM, London WB, Pearson ADJ, and Nagakawa A. The significant dominance of this cluster is explained by the fact that four authors in this cluster are the most productive authors in global NB research.

We utilized Bradford's law for the evaluation of the dispersion of information among scientific journals publishing on NB and identified twenty three (1.2%) core journals that contributed to one third of all NB articles. The majority of these journals (n = 16, 70%) was particularly devoted to the cancer subject, reflecting the highly specific nature of the oncologic specialty. However, although one third of the core journals were not directly cancer-related, the interest of readers and journal editors in Journal of Neurochemistry, Journal of Pediatric Surgery, PLOS One and Neuroscience Letters was also very high, which is reflected in frequent publishing of NB related papers. Moreover, the Journal of Neurochemistry produced the highest number of NB related articles, indicating the high significance of the molecular, cellular and biochemical aspects of NB research.

The most cited paper was the conference-related paper written by Broder GM, containing modifications and clarifications to the International Neuroblastoma Staging System (INSS) and International Neuroblastoma Response Criteria (INRC). An additional three out of the ten most-cited articles were directly linked with the molecular and genetic factors involved in NB tumorigenesis. The identifications of these tumor features has led to improvement of clinical outcomes through the discovery of corresponding druggable targets, such as ganglioside GD2 antibodies. (46) Another four papers were excellent review/seminar articles focusing predominantly on the tumor biology. These reported on the potential for novel targeted treatment options, particularly monoclonal antibodies. (33) However, among the 465 (9.8%) review articles included in our bibliographic dataset, many excellent papers were not included in the top-ten list. This phenomenon is known as the "Matthew Effect": highly cited papers, scientists, and journals are cited more frequently than those with few citations. (47)

The keywords employed most often by authors reflect the dynamics of research hotspots during the study period. We found that the keywords "neuroblastoma" and "apoptosis" were the most common and showed the greatest increase over time. Additionally, all of the top keywords with the strongest citation burst were related to the molecular-biological topics in NB research, suggesting the high significance of this NB sub-field. However, the examination of the field's conceptual structure through a co-word analysis revealed other thematic network clusters, indicating diversity within research sub-fields.

There are some limitations of our study which should be addressed in future scientometric research. First, we used only the Web of Science™ database to search publications, neglecting other search engines such as Scopus, Google Scholar or Index Medicus. Thus, other sources may yield different numbers of research items or citation counts. However, traditional issues of homonymy and synonymy continue to exist, even when utilizing engine machine. (48,49) Second, due to constantly changing citation volumes over time, the results of our study are of temporary nature and valid for the time point of the present study's data extraction (November 12, 2019). Third, the share of non-cited papers should also be considered when determining the h-index and impact factor of the author, article, journal and country. Nevertheless, we believe that our study provides a detailed bibliometric analysis and improves insights into international research on NB.

## Conclusions

This scientometric study provides an in-depth analysis of global neuroblastoma research highlighting the multidisciplinary nature of the NB community. Over the past four decades, NB research has progressed enormously, resulting in better understanding of underlying tumor biology and leading to the development of new molecular therapies. Collaborative research has led to substantial progress in patient stratification and implementation of standardized treatment protocols. Studies like this one are useful for researchers, clinicians, journal editors, and consortiums working on NB in order to understand the strengths and potential gaps in the research and to plan future investments in data collection and science policy. Given the disease burden, especially associated with high-risk NB, a specific analysis of research publications and collaboration networks in this area is warranted to build on the more general scientometric studies.

## Abbreviations

NB Neuroblastoma  
GNB Ganglioneuroblastoma  
GN Ganglioneuroma  
MYCN N-myc proto-oncogene protein  
ALK Anaplastic lymphoma kinase  
CAC Corresponding author's country  
SCP Single country publication  
MCP Multiple countries publications  
TC Total citations  
AAC Average article citations  
h-index Hirsch index  
CI Collaboration index  
MCA Multiple Correspondence Analysis

## Declarations

**Ethics approval and consent to participate:** Not applicable

**Consent for publication:** Not applicable

**Availability of data and material:** The datasets used and analyzed in this study are available from the corresponding author on reasonable request

**Competing interests:** The authors declare that they have no competing interest

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**Authors' contributions:** IM extracted the dataset from Web of Science, performed statistical analysis, and was a major contributor in writing the manuscript. JKF and JS analyzed and interpreted the scientometric data regarding the global research output related to neuroblastoma. All authors read and approved the final manuscript.

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## Supplemental Information

**Fig. S1** The individual profiling of top ten authors regarding to the number of published articles and received total citations (TC) per year. The size of the circles indicate the number of publications per year.

**Fig. S2** Source clustering through Bradford's law and determination of core journals representing the first zone. Core sources include 23 core journals which are responsible for 4,168 articles related to neuroblastoma. The middle and the minor zones are not presented to maximize legibility.

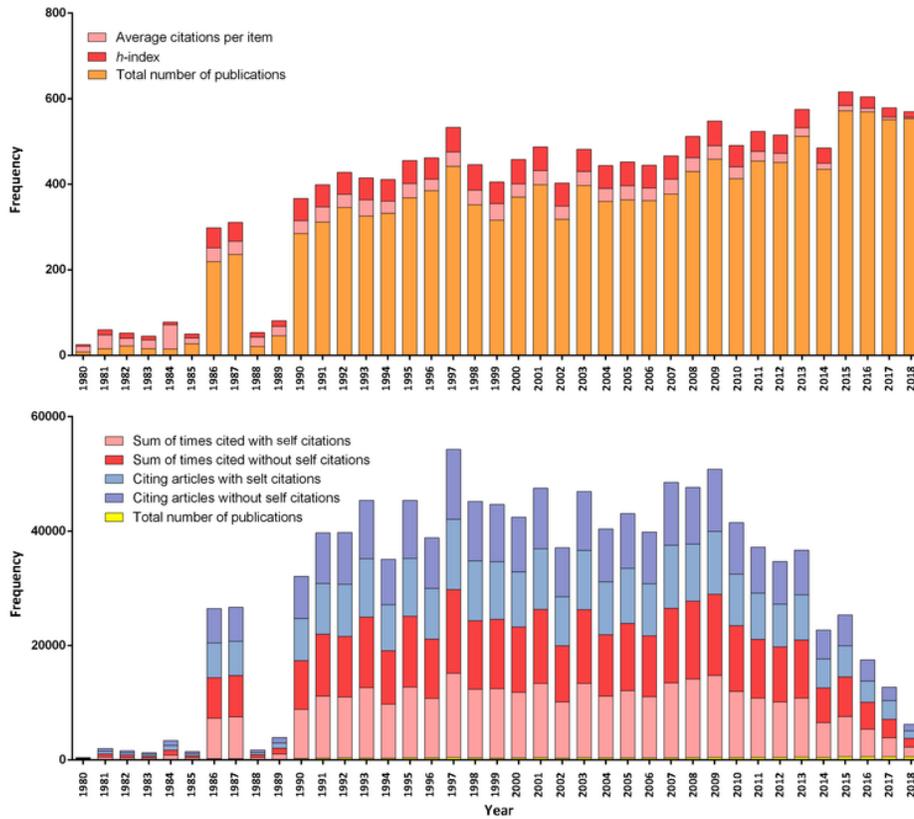
**Fig. S3** A choropleth map detailing the geographic distribution of collaborating countries. The color intensity (from light-blue to dark-blue) is proportional to the number of publications. The number of links (presented as red lines) between any two countries represents the strength of collaboration.

**Fig. S4** Top 10 keywords with the strongest citation bursts during last 38 years

**Fig. S4** Common conceptual frames associated with neuroblastoma studies. Clustering of the 12,435 retrieved articles, including 7 different concepts of clusters of sizes 8, 5, 5, 11, 6, and 2 reflecting concepts frequently linked to neuroblastoma research.

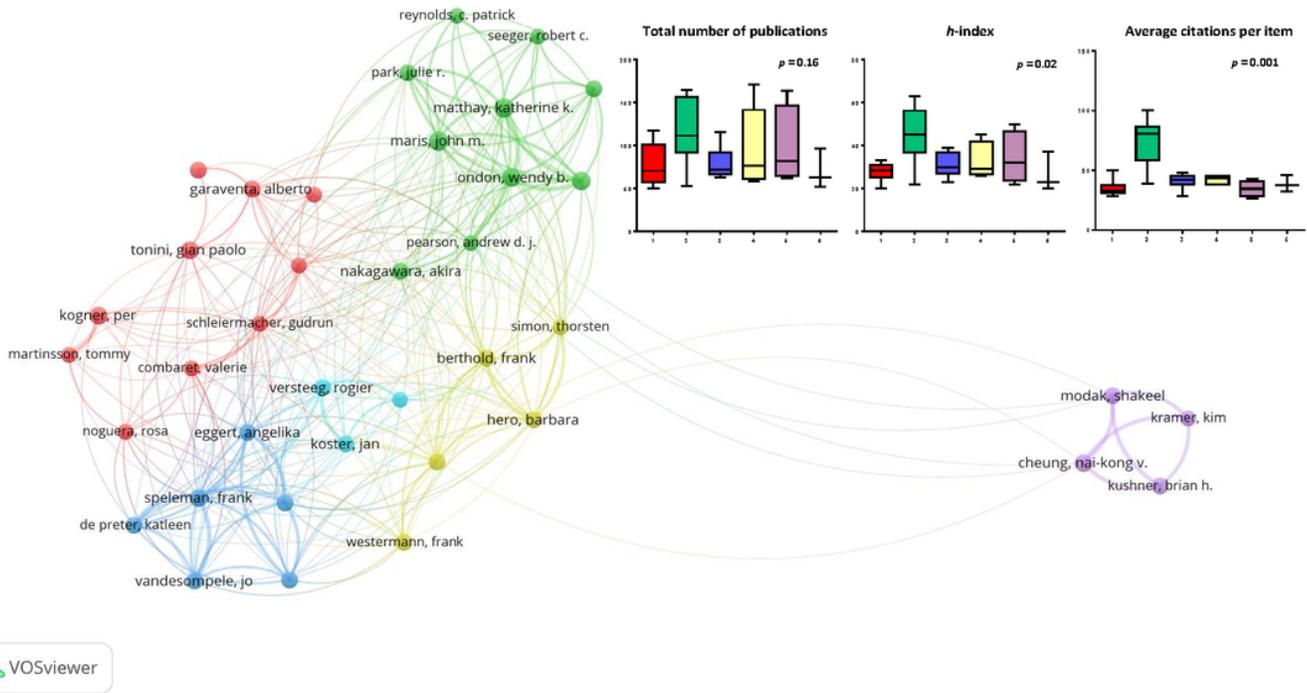
**Fig. S5** The three-fields plot shows the relationship between the author's keywords (research contents, right field), references authors use (intellectual roots, left field), and the top authors (middle field).

## Figures



**Figure 1**

Overall publication and citation performance in neuroblastoma research from 1980 to 2018. The upper panel shows the growth of publications (total number of publications), the average citations they received, and the corresponding h-indices. The lower panel shows the detailed profile of citation dynamics during the last 38 years.



**Figure 2**

The architecture of the co-authorship network based on co-authorship and keyword co-occurrence, analyzed using VOS clustering. The lines indicate collaborations, the thickness represents the strength of collaborations, and the colors indicate clusters. Red corresponds to cluster 1 (CI1 = 10), green corresponds to cluster 2 (CI2 = 10), dark-blue corresponds to cluster 3 (CI3 = 6), yellow corresponds to cluster 4 (CI4 = 5), purple corresponds to cluster 5 (CI5 = 4), light-blue corresponds to cluster 6 (CI6 = 3).



**Figure 3**

The keywords co-occurrence network. Minimum number of occurrence of a keyword = 10, minimum links strength = 10. Overall, 1,638 keywords met threshold criteria. There are 7 clusters of keywords: red indicates Cluster 1 (n=449), green indicates Cluster 2 (n=341), blue indicates Cluster 3 (n=285), yellow indicates Cluster 4 (n=246), purple indicates Cluster 5 (n=214), light-blue indicates Cluster 6 (n=94), orange indicates Cluster 7 (n=9).

## Supplementary Files

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