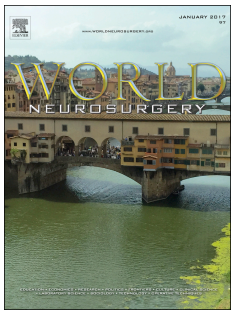

The 100 Most Influential Publications on Medulloblastoma: Areas of Past, Current, and Future Focus

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The 100 Most Influential Publications on Medulloblastoma: Areas of Past, Current, and Future Focus

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Key Words: Medulloblastoma; cerebellar primitive neuroectodermal tumor; PNET

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Abstract

Background: This article is the first to identify the most influential papers on medulloblastoma using the citation analysis methodology.

Objective: To perform a bibliometric analysis of the 100 most cited articles on medulloblastoma.

Methods: Using the Web of Science (WoS) database, search criteria included the title-specific keyword “medulloblastoma” OR “cerebellar primitive neuroectodermal tumor (PNET)” OR “cerebellar PNET”. Publications from 1900-2020 labelled “article”, “review”, “data set”, or “clinical trial” were chosen and ranked based on total number of citations in descending order.

Outcome Measures: Each article was evaluated based on the following variables: total citations, average citations per year (CY), first author, institution of first author, title, publication year, country of origin, SCImago Journal Rank, and Scopus SNIP (Source Normalized Impact per Paper).

Results: Our search yielded 4,928 publications on medulloblastoma. The 100 most-cited publications ranged from 1925-2017 across 42 unique journals; The Journal of Clinical Oncology accounted for the most publications (16%). Paul A. Northcott first-authored the most papers on the list (n=7.7%), while the most widely cited paper was entitled “Altered neural cell fates and medulloblastoma in mouse patched mutants”, authored by Goodrich et al. in *Science* (1997).

Conclusion: As medulloblastoma represents the most common form of pediatric cancerous brain tumor, it is important to identify works that have significantly contributed to the body of knowledge regarding this disease. The 100 most-cited medulloblastoma articles comprise a

significant collection of data regarding the histopathological and molecular classification of medulloblastoma as well as clinical outcomes of therapeutics used to treat this disease.

Introduction

Medulloblastomas are primitive neuroectodermal tumors (PNETs), and due to their location in the cerebellum, are sometimes specifically referred to as cerebellar PNETs.[1] Although these tumors occur in patients of all ages, they are the most prevalent malignant brain tumors in children, with slightly greater prevalence in males, and comprise only 1-2% of adult brain tumors.[2,3] Medulloblastomas typically present with increased intracranial pressure due to their characteristic location within the fourth ventricle.[2] Additionally, as medulloblastomas tend to metastasize, secondary central nervous system (CNS) tumors develop in roughly one-third of patients, and a small subset of patients exhibit extraneural metastases.[4]

Medulloblastoma is often treated with a multi-modal combination of surgery, radiation, or chemotherapy.[5] Due to advances in surgical approaches, nonsurgical therapies, and diagnostic imaging modalities, medulloblastoma is currently curable in approximately 70% of children.[6] However, progression-free survival is less than 50% for children with high-risk medulloblastoma, which remains a significant cause of mortality.[4,7,8] For children with non-disseminated medulloblastoma, five-year survival rate is approximately 80% and many who survive achieve remission.[3] Nonetheless, as many survivors experience significant neurological and cognitive deficits, there is a great need for advancements in the understanding of medulloblastoma biological dynamics and tumor stratification so that treatments can be optimized and individualized in the future.[3]

Histologically, medulloblastomas are categorized based on morphology: classic (CLA), large cell/anaplastic (LCA), desmoplastic/nodular (DN), and medulloblastoma with extensive nodularity (MBEN).[9] Alternatively, as increased grade and extent of anaplasia have been associated with poorer clinical outcomes, a two-tiered anaplastic versus non-anaplastic grading

system has been proposed, and infant medulloblastomas are often stratified by the presence or absence of desmoplastic morphology.[10,11] Furthermore, genomic studies have indicated that there exist 4 subgroups of 12 different medulloblastoma subtypes, including 2 Wnt, 4 Shh, 3 group 3, and 3 group 4 groups - each with their distinct copy-number variations, signaling pathways, and clinical outcomes.[10,12] Although the four subgroups are well-accepted, the degree of overlap between subgroups and the diversity within them is not as well-established.[9] Currently, there are risk stratification biomarkers and clinical trials for therapeutics that incorporate each of the 4 molecular subgroups, however further research is needed to refine management strategies - which include chemotherapy, surgical resection, and cranio-spinal irradiation - for each of the different subtypes.[10]

Over recent years, bibliometric analyses have been used to identify the most influential publications to maximize educational resources for translational scientists and evidence-based practices for clinicians. These analyses measure scholarly impact of individual studies based on the quantity of citations, citation rates, research trends/themes, and the relative impact of both basic science and clinical studies.[13] Prior studies in the neurosurgical and neuro-oncology fields have found that for diffuse intrinsic pontine glioma, clinical progress has been greatly hampered by a still-developing basic science knowledge base[13]; additionally, they have helped analyze trends in tumor immunotherapy and brought those therapies with the greatest potential into focus[14], and have revealed that the past two decades of pediatric neurosurgery research have been centered on “big data” trend/cost analyses, which are often less useful (relative to studies comparing the effectiveness of interventions) for clinical decision-making.[15] By using methods similar to those employed in these informative studies, we aim to perform a bibliometric analysis on medulloblastoma to understand the current state of medulloblastoma research - including a

benchmark of strengths and targets of future focus - and to point towards important developments in our understanding of the disease pathogenesis.

Methods

On March 28, 2020, a title-specific keyword search was performed using the Web of Science (WoS) database to identify the most influential articles on medulloblastoma. As this disease is sometimes termed “cerebellar primitive neuroectodermal tumor (PNET)”, the following search criteria were used for the years 1900 to 2020: “medulloblastoma” OR “cerebellar primitive neuroectodermal tumor” OR “cerebellar PNET”. After these terms were searched using the WoS “All databases” option, the results were arranged according to the number of times each article was cited in descending order. In order to avoid the subjective exclusion of studies from this analysis, all papers from the search were included if they were ranked 1 to 100 in terms of number of total citations. The following variables were then extracted for each article: total number of citations and average number of citations per year (CY), article title, publication year, total citations for each article, article country of origin, and name and institution of first author. In order to quantify relevance, the average citations per year (CY) for each article was calculated as previously described by Jani and colleagues in January 2020, and SCImago Journal Rank (a journal prestige and influence metric) and Scopus SNIP (Source Normalized Impact per Paper), which represents the ratio of a source’s average citations per paper to the citation potential in that source’s specific field [16], were obtained.[17] Previous bibliometric analyses have reported using CY to calculate citation frequency relative to article age in order to correct for the time advantage of older studies.[16,17] Furthermore, articles were classified as belonging to one of three possible categories: basic science, clinical, or literature

review. Basic science papers included those that focused on tumorigenesis in medulloblastoma as well as its molecular classification, while clinical papers reported histopathological results involving patient outcomes in the clinical setting. Any inconsistencies that arose were resolved through clarification with the senior author (RS) and a thorough investigation of the article in full text.

Results

The WoS search for the present study yielded 4,928 publications involving medulloblastoma. The 100 most-cited articles were then selected for review using the "Times Cited" filter on WoS (Table 1). These articles ranged in publication year from 1925-2017; the year which exhibited the greatest number of top 100 cited papers was 2012 (11% of top 100 cited publications) (Figure 1). Notably, a significant proportion of the top 100 papers was published after 1990 (86%); only four papers on the list were published prior to 1970. Additionally, only one paper on the list – published in the year 1925 – is from before 1950. Sorting by decade, the 2000s yielded the most publications (46%), followed by the 2010s (25%) and the 1990s (15%) (Table 2). The top 100 articles on medulloblastoma have been cited a combined a total of 30,873 times, with an average of 308.7 citations per article (Table 1), and a median of 15.6 citations per year (range, 3.14-87.22). Overall, the United States contributed the majority (63%) of articles on this list, followed by Germany (12%), and then Canada (10%) (Figure 2). Notably prolific academic centers included St. Jude Children's Research Hospital (14%), the University of Toronto/ TheHospital for Sick Children (9%), and the German Cancer Research Center (8%). When examining the top 10 articles specifically, citations numbers ranged from 487-1267 citations, and all by one were published after the year 2000.

The most frequently cited article on medulloblastoma is "Altered neural cell fates and medulloblastoma in mouse patched mutants," a basic science study which was published in *Science* in 1997 and has been cited 1,267 times (Table 1). The most prolific author on the top 100 list is Northcott, PA, who has authored seven articles on the top 100 list (Table 3).

Journal of Publication

The list of 100 most cited articles on medulloblastoma includes contributions from 42 different journals, 15 of which have published two or more works related to this topic. The journals that have published the most top cited articles on medulloblastoma include Journal of Clinical Oncology (16%), Nature (9%), Cancer Cell (7%), and Journal of Neurosurgery (6%) (Table 4).

Countries and Institutions

Eleven countries were listed as the location of correspondence for the top 100 articles. The country with the highest contribution of articles was the United States with 63 (63%), followed by Germany (12%) and Canada (10%) (Table 5). The top 3 institutions with the most contributions among the top 100 articles were St. Jude Children's Research Hospital with 14 articles (14%) , University of Toronto/The Hospital for Sick Children with 9 articles (9%), and German Cancer Research Center with 8 articles (8%) (Table 6).

Article Category

Among the top 100 articles, most were categorized as basic science (n=47), followed by clinical (n=42) and then literature review (n=11) (Table 7, Figure 3). Of the top 10 articles, 5

were categorized as basic science, 4 as clinical, and 1 as a literature review. The most-cited basic science article was also the most cited article overall (previously mentioned above), and ranked 6th in CY with 52.8. The most-cited clinical article was "Brief Report: Treatment of Medulloblastoma with Hedgehog Pathway Inhibitor GDC-0449" published in *New England Journal of Medicine,* and it ranked 3rd overall in both total citations (727) and CY (60.58) (Table 1). The top 100 articles were also classified according to the following topics: 1) cellular and molecular biology (Table 8), 2) genetics (Table 9), and therapeutics and/or clinical outcomes (Table 10).

Authors

In an analysis of the top 100 articles, the most prolific author was Paul A. Northcott, who published 7 articles, followed by Roger J. Packer (who published 4), and RJ Gilbertson (3) (Table 3). Of Northcott's articles, 1 (14.3%) was clinical, 5 (71.4%) were basic science, and 1 (14.3%) was a review. A majority of his articles (n=5, 71.4%) were published in a Nature family journal and discussed the genetic correlates of medulloblastoma.

Discussion

Bibliometric analyses can help provide insight into the status of research within a particular field, identify strengths of research and areas where it is lacking, and highlight articles that can assist researchers, trainees, and clinicians.[16] To the authors' knowledge, the present study is the first bibliometric analysis to identify the most impactful studies, individuals, institutions, and research disciplines with respect to medulloblastoma. It identifies the top 100

articles based on citation count, and evaluates the publication impact of each by calculating additional metrics including CY, SCImago Journal Rank, and Scopus SNIP.

It is unsurprising that the top 100 articles on medulloblastoma are published across 42 unique journals, as research on medulloblastoma comprises a complex, dynamic, and multidisciplinary field. The most cited study overall – Goodrich et al's "Altered neural cell fates and medulloblastoma in mouse patched mutants," – was published in *Science* in 1997 and received the 6th most CY (52.79).[18] While total citation count might indicate that an article has historical – but not recent – importance, CY is the primary measure of current relevance independent of an article's time in circulation.[16] Because Goodrich's 1997 study is 6th highest in CY, its total citation count likely stems from both its current and historical relevance. This basic science article examines the effects of inactivating PATCHED (PTC) gene mutations on embryogenesis and tumorigenesis in mice. Interestingly, PTC is a human tumor suppressor gene (and component of the Hedgehog (SHH) signaling pathway) that, when mutated, increases risk of developmental defects, basal cell carcinoma, and brain tumors in patients with basal cell nevus syndrome (BCNS).[18] In Goodrich's study, homozygous PTC mutations proved fatal, while mice heterozygous for the mutant allele displayed a phenotype similar to that seen in BCNS , including limb defects and cerebellar medulloblastomas.[18] As such, Goodrich and colleagues reported that PTC is a key regulator of growth and pattern formation during neurogenesis and in the adult cerebellum, and that the SHH-PTC pathway could be of direct relevance to medulloblastoma diagnostics and therapeutics.[18] Ultimately, their pioneering work is among the original works which eventually lead to identification of the SHH medulloblastoma subgroup; it has since been found that germline PTC mutations are responsible for Gorlin syndrome, which predisposes individuals to medulloblastoma.[19]

In the time since Goodrich's basic science study, general consensus has formed around the existence of four medulloblastoma subgroups. These four groups are outlined in the 2nd most-cited study, "Molecular subgroups of medulloblastoma: the current consensus", and the study with the 2nd highest CY, "Medulloblastoma Comprises Four Distinct Molecular Variants" by Northcott and colleagues. The former study, which was published by Taylor and colleagues in *Acta Neuropathologica* in 2012, was the most cited literature review article in the top 100, with 785 total citations since 2012, and also exhibited the highest CY (87.22) of all studies. Essentially, it contextualized and established the molecular classification scheme proposed by Northcott in their 2011 study.[12] Through a genomics and transcriptional profiling analysis, Northcott and colleagues proposed a 4 subgroup tumor classification system based on variations in genetic events, immunohistochemistry, and prognosis: WNT, SHH, Group 3, and Group 4.[12] Paul Northcott's contributions to the field both as a student and as an independent researcher were significant because they laid the groundwork for the design of future risk-targeted therapies based on the gene mutations and prognostic factors associated with each subgroup.[12] In the literature review that followed, Taylor and colleagues solidified Northcott's classification scheme by declaring consensus as to the existence of four molecular subgroups, which they predicted would continue to evolve and inform care for medulloblastoma patients.[19] This review article's high total citation ranking and CY suggests that it has been useful for researchers, clinicians, and trainees alike, however this is also a reflection of the impact of prior advancements contributed by primary clinical and basic science research articles that are lower on the list.

Including this 2012 study, Taylor has published two articles in the top 10 most-cited (2nd and 7th overall). According to the article that ranks 7th by citation count, "Mutations in SUFU

predispose to medulloblastoma", germline SUFU (a negative regulator in the SHH-PTC pathway) mutations genetically predispose infants to medulloblastoma in the first years of life with worse prognosis than is normally observed for SHH subgroup medulloblastomas. Given that SHH medulloblastomas are already categorized as high risk, Taylor et al suggested the use of even more intensive chemotherapies for patients with the higher risk SUFU germline mutation.[20] At the time, SUFU was a newly-identified tumor suppressor gene, and this study highlights the surge of basic science medulloblastoma research investigating molecular dynamics that occurred following Goodrich's 1997 report on the SHH-PTL pathway.[20] Indeed, this surge corresponds to the outpouring of medulloblastoma studies which occurred during the 2000s, the most prolific decade to date with respect to medulloblastoma research.

Another important article to highlight is Packer and colleagues' "Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma", is the 10th most-cited study on medulloblastoma.[21] Published in 2006 in the *Journal of Clinical Oncology*, it was - at the time of its publication - the largest prospective randomized controlled trial ever performed for pediatrics medulloblastoma patients, and reported a "favorable" event-free survival rate for pediatric non-disseminated medulloblastoma treated with reduced-dose craniospinal radiation and chemotherapy.[21] Additionally, Packer et al. suggested the use of chemotherapy for all pediatric medulloblastoma patients, and their use of reduced-dose radiation therapy has continued to inform risk-stratified clinical trials (which seek to determine when craniospinal radiation can be avoided in pediatric patients) in the years after the establishment of the four medulloblastoma subgroups.[21,22]

More recently, Cavalli and colleagues – in "Intertumoral Heterogeneity within Medulloblastoma Subgroups", which ranks 74th and 13th in total citations and CY, respectively –

expanded upon previous classifications to identify 12 medulloblastoma subtypes using their similarity network fusion (SNF) cluster analysis of genome-wide DNA methylation and gene expression[10]. These included two WNT, four SHH, three group 3, and three group 4 subtypes.[10] As improved subtype characterization can aid clinicians and researchers in drug selection, outcome prediction, novel therapeutic development, and risk stratification biomarker identification, the Taylor and Cavalli classification studies have proven paramount to the development of clinical trials in recent years.[10,19] For example, Robinson and colleagues recently reported results of a multicenter, Phase II clinical trial which investigated the effect of a risk-adapted therapeutic approach on survival in a large cohort of pediatric medulloblastoma patients.[23] They reported that the SHH subgroup exhibited higher progression-free survival compared to the group 3 subgroup, and that within the SHH subgroup, the iSHH-II subtype showed improved progression-free survival (when not treated with radiation or intraventricular/high-dose chemotherapy) as compared to the iSHH-I subtype.[23] By laying the foundation for the development of risk-stratified therapies, the classification systems imparted but Taylor and Cavalli have demonstrated the importance of medulloblastoma molecular tumor classification, possibly demonstrating why basic science studies have predominated to this point. Of the top 10 most-cited articles, 5 were classified as basic science studies, 4 were clinical reports, and 1 was a literature review. A similar trend was noted in the top 20 most-cited articles, as 10 were basic science reports, 6 were clinical studies, and 4 were literature reviews. In total, 47% of all studies were classified as basic science research, highlighting the fact that the molecular underpinnings of medulloblastoma - although largely identified - have not been resolved.[9] As the DNA methylation patterns, histone modifications, chromatin remodeling features, genomic structural variations, and proteomics of each subgroup are uncovered, clinical

studies investigating precision therapies will be increasingly well-informed going forward.[9] In fact, as a result of advances in cancer genomics, single-cell sequencing and tumor models[9], they will likely supplant basic science studies as the focus of medulloblastoma research becomes increasingly translational (and they are already a close 2nd, comprising 42% of the 100 most-cited studies).

Finally, many of the oldest studies included in this analysis, including the 1925 study by Bailey et al., continue to be cited because they established the framework of medulloblastoma symptomology, etiology, and diagnosis. Landmark studies such as this have a great deal of historical significance and established clear diagnostic principles that continue to guide modern patient management.

Limitations

Due to the nature of this study's design, there are several possible limitations that must be brought to light. First and foremost, it is important to acknowledge that citation number is not a definitive measure of article importance or quality, and that this method can potentially lead to bias. For example, an inherent bias associated with ranking the top 100 medulloblastoma papers by citation is that it can skew results towards favoring earlier publications, as they have had more time to accrue citations than recent articles.[24] In response to this potential bias, CY (Table 1) for each article have been reported, as these values may be more indicative of publication relevance.[17] However, a potential confound that remains is due to the "obliteration by incorporation" effect, in which well-established knowledge from older, original articles is no longer cited.[17] Next, the title-specific search performed through Web of Science in the present study could have resulted in the erroneous exclusion of qualifying papers from the 100 most-

cited list, including those from non-indexed journals, books, and other reports.[25] More specifically, the Web of Science is not all-encompassing and only contains journal articles published in English; however, its use as a database for bibliometric analyses is well established.[24,26] Additionally, the present study rests upon the logical assumption that any publication relevant to medulloblastoma will contain the terms "medulloblastoma" or "cerebellar primitive neuroectodermal tumor" or "cerebellar PNET" within its title. Finally, in evaluating contributing authors and institutions, only first authors and their respective institutions were included. As a result, our study may not have identified secondary authors and/or contributing institutions in multicenter studies that have had a significant impact on medulloblastoma research. Lastly, our review of medulloblastoma literature was comprehensive and ranged almost a century. As a result, it is possible that some studies included in our review are legacy studies that may be cited through common practice and deference to our history. However, the authors opted to include these studies because they highlight the evolution of medulloblastoma research and spotlight trends in citation strategies within the field. Regardless of these potential limitations, the present study remains, to the authors' knowledge, the only to perform bibliometric analysis on medulloblastoma.

Conclusion

As the only article which has identified the 100 most influential articles on medulloblastoma, the present study can aid researchers, trainees, and clinicians alike in selecting well-established sources related to this disease. Because medulloblastoma is the most common cancerous tumor in childhood, it will continue to be investigated by future researchers, who can reference our report in order to quickly retrieve relevant information. Reflecting nearly a century's worth of publications, the 100 most cited medulloblastoma articles were published in

42 unique journals, owing to the diverse and multidisciplinary nature of care for this disease. Although basic science research has proven crucial in unearthing the complex molecular classification of this extremely heterogeneous tumor, there is a great need for clinical trials to eventually supplant basic science studies as the focus of medulloblastoma research. However, until the four molecular variants and their numerous subtypes are better characterized, basic science studies will continue to be instrumental in informing the next wave of targeted therapies.

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Figure Legend

Table 1. Top 100 papers on medulloblastoma by citation number

Figure 1. Trends in the top 100 most cited medulloblastoma article publications by decade.

Table 2. The number of publications per decade for the top 100 most highly cited articles.

Figure 2. Percent distribution of the most cited articles by country of origin.

Table 3. The frequency of authors who contributed 2 or more articles.

Table 4. The journal of publications in which the top 100 most cited articles were published.

Table 5. Countries of origin for the top cited papers on medulloblastoma.

Table 6. Top contributing institutions based on first author

Table 7. Category type of the 100 most cited articles.

Figure 3. Percentage distribution by article category for the top 100 articles.

Table 8. List of the studies investigating cellular and molecular biology

Table 9. List of the studies investigating genetics

Table 10. List of the studies investigating therapeutics and/or clinical outcomes

Table 1. Top 100 papers on medulloblastoma by citation number

Rank by Total Citations	Rank by Average Citations per Year	Title	Authors	Journal Title	Year of Publication	Total Citations	Average Citations per Year	Country	Type of Study
1	6	Altered neural cell fates and medulloblastoma in mouse patched mutants	Goodrich, LV	SCIENCE	1997	1267	52.79	USA	Basic Science
2	1	Molecular subgroups of medulloblastoma: the current consensus	Taylor, Michael D.	ACTA NEUROPATHOLOGICA	2012	785	87.22	Canada	Review
3	3	Brief Report: Treatment of Medulloblastoma with Hedgehog Pathway Inhibitor GDC-0449.	Rudin, Charles M.	NEW ENGLAND JOURNAL OF MEDICINE	2009	727	60.58	USA	Clinical
4	2	Medulloblastoma Comprises Four Distinct Molecular Variants	Northcott, Paul A.	JOURNAL OF CLINICAL ONCOLOGY	2011	700	70	Canada	Clinical
5	20	Medulloblastoma growth inhibition by Hedgehog pathway	Berman, DM	SCIENCE	2002	659	34.68	USA	Basic Science

		blockade							
6	8	Smoothened Mutation Confers Resistance to a Hedgehog Pathway Inhibitor in Medulloblastoma	Yauch, Robert L.	SCIENCE	2009	605	50.42	USA	Basic Science
7	29	Mutations in SUFU predispose to medulloblastoma	Taylor, MD	NATURE GENETICS	2002	547	28.79	Canada	Basic Science
8	21	Risk-adapted craniospinal radiotherapy followed by high-dose chemotherapy and stem-cell rescue in children with newly diagnosed medulloblastoma (St Jude Medulloblastoma-96): long-term results from a prospective,	Gajjar, Amar	LANCET ONCOLOGY	2006	500	33.33	USA	Clinical

		multicentre trial							
9	10	The Genetic Landscape of the Childhood Cancer Medulloblastoma	Parsons, D. Williams	SCIENCE	2011	499	49.9	USA	Basic Science
10	22	Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma	Packer, Roger J.	JOURNAL OF CLINICAL ONCOLOGY	2006	487	32.47	USA	Clinical
11	4	Dissecting the genomic complexity underlying medulloblastoma	Jones, David T. W.	NATURE	2012	481	53.44	Germany	Basic Science

12	5	Molecular subgroups of medulloblastoma: an international meta-analysis of transcriptome, genetic aberrations, and clinical data of WNT, SHH, Group 3, and Group 4 medulloblastomas	Kool, Marcel	ACTA NEUROPATHOLOGICA	2012	477	53	Germany	Review
13	16	Targeting brain cancer: advances in the molecular pathology of malignant glioma and medulloblastoma	Huse, Jason T.	NATURE REVIEWS CANCER	2010	462	42	USA	Review
14	64	THE CEREBELLAR MEDULLOBLASTOMA AND ITS RELATIONSHIP TO PRIMITI	RORKE, LB	JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY	1983	458	12.05	USA	Review

		VE NEUROECTODERMAL TUMORS							
15	7	Novel mutations target distinct subgroups of medulloblastoma	Robinson, Giles	NATURE	2012	456	50.67	USA	Basic Science
16	39	Metastasis stage, adjuvant treatment, and residual tumor are prognostic factors for medulloblastoma in children: Conclusions from the Children's Cancer Group 921 randomized phase III study	Zeltzer, PM	JOURNAL OF CLINICAL ONCOLOGY	1999	453	20.59	USA	Clinical
17	19	Integrated Genomics Identifies Five Medulloblastoma Subtypes with Distinct Genetic Profiles, Pathway	Kool, Marcel	PLOS ONE	2008	452	34.77	Netherlands	Clinical

		Signatures and Clinicopathological Features							
18	26	Genomics identifies medulloblastoma subgroups that are enriched for specific genetic alterations	Thompson, MC	JOURNAL OF CLINICAL ONCOLOGY	2006	452	30.13	USA	Basic Science
19	9	Medulloblastoma exome sequencing uncovers subtype-specific somatic mutations	Pugh, Trevor J.	NATURE	2012	451	50.11	USA	Basic Science
20	11	Genome Sequencing of Pediatric Medulloblastoma Links Catastrophic DNA Rearrangements with TP53 Mutations	Rausch, Tobias	CELL	2012	447	49.67	Germany	Basic Science

21	33	Treatment of early childhood medulloblastoma by postoperative chemotherapy alone	Rutkowski, S	NEW ENGLAND JOURNAL OF MEDICINE	2005	447	27.94	Germany	Clinical
22	12	Subgroup-specific structural variation across 1,000 medulloblastoma genomes	Northcott, Paul A.	NATURE	2012	432	48	Canada	Basic Science
23	18	Subtypes of medulloblastoma have distinct developmental origins	Gibson, Paul	NATURE	2010	430	39.09	USA	Basic Science
24	55	THE TREATMENT OF MEDULLOBLASTOMA - RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL	EVANS, AE;	JOURNAL OF NEUROSURGERY	1990	430	13.87	USA	Clinical

		OF RADIATION-THERAPY WITH AND WITHOUT CCNU, VINCRISTINE, AND PREDNISONE							
25	36	Suppression of the Shh pathway using a small molecule inhibitor eliminates medulloblastoma in Ptc1(+/-) p53(-/-) mice	Romer, JT	CANCER CELL	2004	406	23.88	USA	Basic Science
26	17	Integrative Genomic Analysis of Medulloblastoma Identifies a Molecular Subgroup That Drives Poor Clinical Outcome	Cho, Yoon-Jae	JOURNAL OF CLINICAL ONCOLOGY	2011	396	39.6	USA	Basic Science

27	25	Medulloblastoma can be initiated by deletion of patched in lineage-restricted progenitors or stem cells	Yang, Zeng-Jie	CANCER CELL	2008	394	30.31	Australia	Basic Science
28	30	Acquisition of granule neuron precursor identity is a critical determinant of progenitor cell competence to form Shh-induced medulloblastoma	Schueller, Ulrich	CANCER CELL	2008	365	28.08	USA	Basic Science
29	85	TREATMENT AND PROGNOSIS OF MEDULLOBLASTOMA IN CHILDREN - A STUDY OF 82 VERIFIED CASES	BLOOM, HJG	AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE	1969	362	6.96	USA	Clinical

30	98	Medulloblastoma cerebelli - A common type of midcerebellar glioma of childhood	Bailey, P	ARCHIVES OF NEUROLOGY AND PSYCHIATRY	1925	359	3.74	USA	Clinical
31	59	OUTCOME FOR CHILDREN WITH MEDULLOBLASTOMA TREATED WITH RADIATION AND CISPLATIN, CCNU, AND VINCRISTINE CHEMOTHERAPY	PACKER, RJ	JOURNAL OF NEUROSURGERY	1994	347	12.85	USA	Clinical
32	48	Expression profiling of medulloblastoma: PDGFRA and the RAS/MAPK pathway as therapeutic targets for metastatic disease	MacDonald, TJ	NATURE GENETICS	2001	336	16.8	USA	Basic Science

33	34	PI3K pathway regulates survival of cancer stem cells residing in the perivascular niche following radiation in medulloblastoma in vivo	Hambardzumyan, Dolores	GENES & DEVELOPMENT	2008	332	25.54	USA	Basic Science
34	27	Interfering with Resistance to Smoothened Antagonists by Inhibition of the PI3K Pathway in Medulloblastoma	Buonamici, Silvia	SCIENCE TRANSLATIONAL MEDICINE	2010	328	29.82	USA	Basic Science
35	50	Intellectual outcome after reduced-dose radiation therapy plus adjuvant chemotherapy for medulloblastoma : A children's cancer group	Ris, MD	JOURNAL OF CLINICAL ONCOLOGY	2001	323	16.15	USA	Clinical

		study							
36	76	ADJUVANT CHEMOTHERAPY FOR MEDULLOBLASTOMA - THE 1ST MULTICENTER CONTROL TRIAL OF THE INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY (SIOP I)	TAIT, DM	EUROPEAN JOURNAL OF CANCER	1990	321	10.35	England	Clinical
37	28	Hedgehog beyond medulloblastoma and basal cell carcinoma	Teglund, Stephan	BIOCHIMICA ET BIOPHYSICA ACTA-REVIEWS ON CANCER	2010	317	28.82	Sweden	Basic Science
38	15	Genome Sequencing of SHH Medulloblastoma Predicts Genotype-Related Response to Smoothened Inhibition	Kool, Marcel	CANCER CELL	2014	314	44.86	Germany	Basic Science

39	56	Atypical teratoid/rhabdoid tumor of the central nervous system: A highly malignant tumor of infancy and childhood frequently mistaken for medulloblastoma - A pediatric oncology group study	Burger, PC	AMERICAN JOURNAL OF SURGICAL PATHOLOGY	1998	307	13.35	USA	Clinical
40	35	Multiple recurrent genetic events converge on control of histone lysine methylation in medulloblastoma	Northcott, Paul A.	NATURE GENETICS	2009	298	24.83	Canada	Basic Science
41	45	beta-catenin status predicts a favorable outcome in childhood medulloblastoma: The United Kingdom	Ellison, DW	JOURNAL OF CLINICAL ONCOLOGY	2005	290	18.13	England	Clinical

		Children's Cancer Study Group Brain Tumour Committee							
42	31	Medulloblastoma: clinicopathological correlates of SHH, WNT, and non-SHH/WNT molecular subgroups	Ellison, David W.	ACTA NEUROPATHOLOGICA	2011	280	28	USA	Clinical
43	24	Clonal selection drives genetic divergence of metastatic medulloblastoma	Wu, Xiaochong	NATURE	2012	279	31	Canada	Basic Science
44	58	Postoperative neoadjuvant chemotherapy before radiotherapy as compared to immediate radiotherapy followed by maintenance chemotherapy in the	Kortmann, RD	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2000	274	13.05	Germany	Clinical

		treatment of medulloblastoma in childhood: Results of the German prospective randomized trial HIT '91							
45	68	Neuropsychologic functioning of survivors of childhood medulloblastoma randomized to receive conventional or reduced-dose craniospinal irradiation: A Pediatric Oncology Group Study	Mulhern, RK	JOURNAL OF CLINICAL ONCOLOGY	1998	266	11.57	USA	Clinical
46	60	Loss of p53 but not ARF accelerates medulloblastoma in mice heterozygous for patched	Wetmore, C	CANCER RESEARCH	2001	257	12.85	USA	Basic Science

47	88	MEDULLOBLASTOMA IN CHILDHOOD - SURVIVAL AND FUNCTIONAL RESULTS	HIRSCH, JF	ACTA NEUROCHIRURGICA	1979	254	6.05	Austria	Clinical
48	86	MEDULLOBLASTOMA - CLINICAL PRESENTATION AND MANAGEMENT - EXPERIENCE AT THE HOSPITAL-FOR-SICK-CHILDREN, TORONTO, 1950-1980	PARK, TS	JOURNAL OF NEUROSURGERY	1983	248	6.53	USA	Clinical
49	40	Identification of CD15 as a Marker for Tumor-Propagating Cells in a Mouse Model of Medulloblastoma	Read, Tracy-Ann	CANCER CELL	2009	241	20.08	USA	Basic Science

50	65	Patterns of intellectual development among survivors of pediatric medulloblastoma: A longitudinal analysis	Palmer, SL	JOURNAL OF CLINICAL ONCOLOGY	2001	240	12	USA	Clinical
51	57	Medulloblastoma: signalling a change in treatment	Gilbertson, RJ	LANCET ONCOLOGY	2004	227	13.35	USA	Review
52	42	MicroRNA profiling in human medulloblastoma	Ferretti, Elisabetta	INTERNATIONAL JOURNAL OF CANCER	2009	226	18.83	Italy	Basic Science
53	53	Neurocognitive consequences of risk-adapted therapy for childhood medulloblastorna	Mulhern, RK	JOURNAL OF CLINICAL ONCOLOGY	2005	226	14.13	USA	Clinical
54	43	Dual and opposing roles of primary cilia in medulloblastoma	Han, Young-Goo	NATURE MEDICINE	2009	225	18.75	USA	Basic Science

		development							
55	51	Oxysterols stimulate Sonic hedgehog signal transduction and proliferation of medulloblastoma cells	Corcoran, Ryan B.	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	2006	225	15	USA	Basic Science
56	69	Antitumor activity of the rapamycin analog CCI-779 in human primitive neuroectodermal tumor/medulloblastoma models as single agent and in combination chemotherapy	Geoerger, B	CANCER RESEARCH	2001	221	11.05	USA	Basic Science

57	92	RADIATION TREATMENT FOR MEDULLOBLASTOMA - A 21-YEAR REVIEW	BERRY, MP	JOURNAL OF NEUROSURGERY	1981	221	5.53	Canada	Clinical
58	63	Results of a randomized study of preradiation chemotherapy versus radiotherapy alone for nonmetastatic medulloblastoma: The International Society of Paediatric Oncology United Kingdom Children's Cancer Study Group PNET-3 study	Taylor, RE	JOURNAL OF CLINICAL ONCOLOGY	2003	219	12.17	England	Clinical
59	23	Enhancer hijacking activates GFI1 family oncogenes in medullobl	Northcott, Paul A.	NATURE	2014	218	31.14	Germany	Basic Science

		astoma							
60	46	The miR-17 similar to 92 cluster collaborates with the Sonic Hedgehog pathway in medulloblastoma	Uziel, Tamar	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	2009	215	17.92	USA	Basic Science
61	47	Outcome Prediction in Pediatric Medulloblastoma Based on DNA Copy-Number Aberrations of Chromosomes 6q and 17q and the MYC and MYCN Loci	Pfister, Stefan	JOURNAL OF CLINICAL ONCOLOGY	2009	213	17.75	Germany	Clinical
62	95	MEDULLOBLASTOMA - REPORT OF 201 CASES WITH EMPHASIS ON RELATIO	CHATTY, EM	CANCER	1971	213	4.26	USA	Clinical

		NSHIP OF HISTOLOGIC VARIANTS TO SURVIVAL							
63	80	PROSPECTIVE RANDOMIZED TRIAL OF CHEMOTHERAPY GIVEN BEFORE RADIOTHERAPY IN CHILDHOOD MEDULLOBLASTOMA - INTERNATIONAL-SOCIETY-OF-PEDIATRIC-ONCOLOGY (SIOP) AND THE (GERMAN)-SOCIETY-OF-PEDIATRIC-ONCOLOGY (GPO) -	BAILEY, CC	MEDICAL AND PEDIATRIC ONCOLOGY	1995	210	8.08	England	Clinical

		SIOP-II							
64	75	Risks of young age for selected neurocognitive deficits in medulloblastoma are associated with white matter loss	Mulhern, RK	JOURNAL OF CLINICAL ONCOLOGY	2001	208	10.4	USA	Clinical
65	78	Prognostic significance of HER2 and HER4 coexpression in childhood medulloblastoma	Gilbertson, RJ	CANCER RESEARCH	1997	206	8.58	England	Clinical
66	99	MULTIPLE BASAL-CELL NEVI SYNDROME - AN ANALYSIS OF A SYNDROME CONSISTING OF	GORLIN, RJ	CANCER	1965	206	3.68	USA	Review

		MULTIPLE NEVOID BASAL-CELL CARCINOMA JAW CYSTS SKELETAL ANOMALIES MEDULLOBLASTOMA AND HYPORESPONSIVENESS TO PARATHORMONE							
67	83	EXPRESSION OF THE NEUROTROPHIN RECEPTOR TRKC IS LINKED TO A FAVORABLE OUTCOME IN MEDULLOBLASTOMA	SEGAL, RA	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	1994	201	7.44	USA	Clinical

68	66	Clinical, histopathologic, and molecular markers of prognosis: Toward a new disease risk stratification system for medulloblastoma	Gajjar, A	JOURNAL OF CLINICAL ONCOLOGY	2004	199	11.71	USA	Clinical
69	67	Advantage of protons compared to conventional X-ray or IMRT in the treatment of a pediatric patient with medulloblastoma	St Clair, WH	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2004	198	11.65	USA	Clinical
70	49	MicroRNA-199b-5p Impairs Cancer Stem Cells through Negative Regulation of HES1 in Medulloblastoma	Garzia, Livia	PLOS ONE	2009	197	16.42	Italy	Basic Science

71	54	Daoy medulloblastoma cells that express CD133 are radioresistant relative to CD133- cells, and the CD133+ sector is enlarged by hypoxia	Blazek, Ed R.	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2007	197	14.07	USA	Basic Science
72	32	Decoding the regulatory landscape of medulloblastoma using DNA methylation sequencing	Hovestadt, Volker	NATURE	2014	196	28	Germany	Basic Science
73	38	Rapid, reliable, and reproducible molecular sub-grouping of clinical medulloblastoma samples	Northcott, Paul A.	ACTA NEUROPATHOLOGICA	2012	191	21.22	Canada	Basic Science

74	13	Intertumoral Heterogeneity within Medulloblastoma Subgroups	Cavalli, Florence M. G.	CANCER CELL	2017	190	47.5	Canada	Clinical
75	89	A MUSCLE ACETYLCHOLINE-RECEPTOR IS EXPRESSED IN THE HUMAN CEREBELLAR MEDULLOBLASTOMA CELL-LINE TE671	LUTHER, MA	JOURNAL OF NEUROSCIENCE	1989	188	5.88	USA	Basic Science
76	94	ESTABLISHMENT OF A HUMAN MEDULLOBLASTOMA CELL-LINE AND ITS HETEROTRANSPLANTATION INTO NUDE-MICE	JACOBSEN, PF	JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY	1985	188	5.22	Australia	Basic Science

77	91	STRUCTURAL CHROMOSOMAL-ABNORMALITIES IN HUMAN MEDULLOBLASTOMA	BIGNER, SH	CANCER GENETICS AND CYTOGENETICS	1988	187	5.67	USA	Basic Science
78	62	Incidence and severity of postoperative cerebellar mutism syndrome in children with medulloblastoma: a prospective study by the Children's Oncology, Group	Robertson, Patricia L.	JOURNAL OF NEUROSURGERY	2006	186	12.4	USA	Clinical
79	84	Effects of medulloblastoma resections on outcome in children: A report from the children's cancer group	Albright, AL	NEUROSURGERY	1996	185	7.4	USA	Clinical

80	52	The origins of medulloblastoma subtypes	Gilbertson, Richard J.	ANNUAL REVIEW OF PATHOLOGY-MECHANISMS OF DISEASE	2008	184	14.15	USA	Review
81	87	THE INCIDENCE OF GORLIN SYNDROME IN 173 CONSECUTIVE CASES OF MEDULLOBLASTOMA	EVANS, DGR	BRITISH JOURNAL OF CANCER	1991	184	6.13	England	Clinical
82	14	The whole-genome landscape of medulloblastoma subtypes	Northcott, Paul A.	NATURE	2017	180	45	Germany	Basic Science
83	73	Sonic hedgehog and insulin-like growth factor signaling synergize to induce medulloblastoma	Rao, G	ONCOGENE	2004	179	10.53	USA	Basic Science

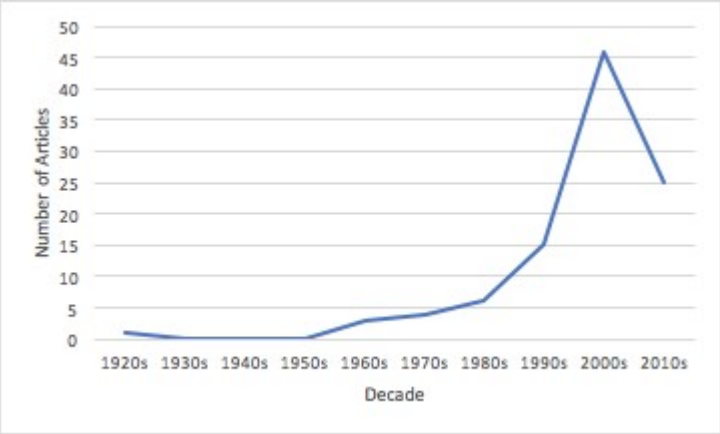
		formation from nestin-expressing neural progenitors in mice							
84	100	MEDULLOBLASTOMA + SO-CALLED ARACHNOIDAL CEREBELLAR SARCOMA	RUBINSTEIN, LJ	BRAIN	1964	179	3.14	USA	Clinical
85	70	Genomic and protein expression profiling identifies CDK6 as novel independent prognostic marker in medulloblastoma	Mendrzyk, F	JOURNAL OF CLINICAL ONCOLOGY	2005	176	11	Germany	Basic Science
86	96	MEDULLOBLASTOMA IN CHILDREN - CORRELATION BETWEEN STAGING AND	HARISIADIS, L	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY	1977	176	4	USA	Clinical

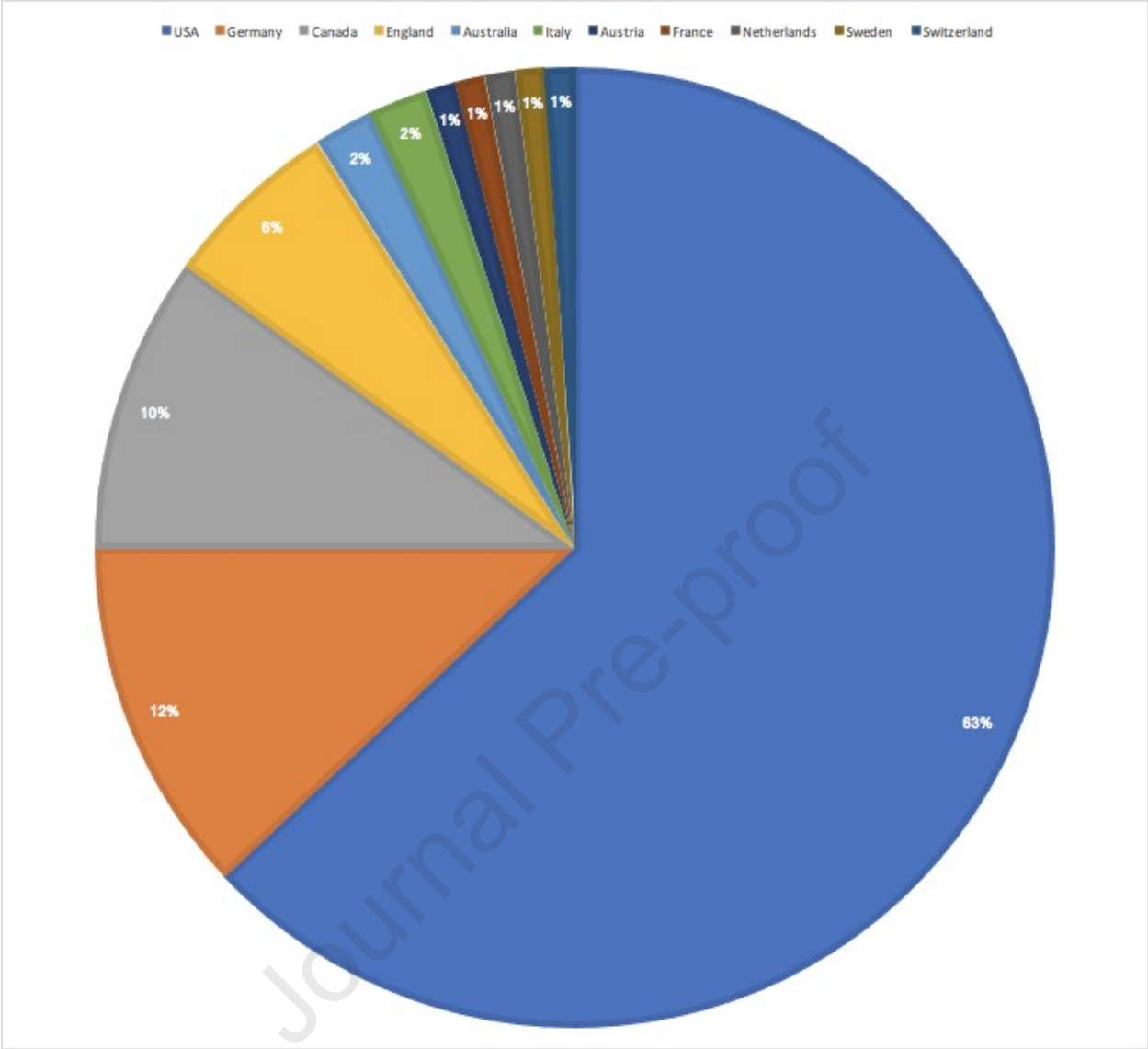
		RESULTS OF TREATMENT		PHYSICS					
87	77	Intensity-modulated radiation therapy for pediatric medulloblastoma: Early report on the reduction of ototoxicity	Huang, E	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2002	175	9.21	USA	Clinical
88	81	Medulloblastoma: clinical and biologic aspects.	Packer, R J	Neuro-oncology	1999	175	7.95	USA	Review
89	61	Medulloblastoma in childhood: new biological advances	Crawford, John R.	LANCET NEUROLOGY	2007	174	12.43	USA	Review
90	97	ESTABLISHMENT OF A HUMAN MEDULLOBLASTOMA CELL LINE	MCALLISTER, RM	INTERNATIONAL JOURNAL OF CANCER	1977	174	3.95	USA	Basic Science

91	41	The clinical implications of medulloblastoma subgroups	Northcott, Paul A.	NATURE REVIEWS NEUROLOGY	2012	173	19.22	Canada	Review
92	71	Treatment of medulloblastoma with postoperative chemotherapy alone: an SFOP prospective trial in young children	Grill, J	LANCET ONCOLOGY	2005	173	10.81	France	Clinical
93	90	IMPROVED SURVIVAL WITH THE USE OF ADJUVANT CHEMOTHERAPY IN THE TREATMENT OF MEDULLOBLASTOMA	PACKER, RJ	JOURNAL OF NEUROSURGERY	1991	172	5.73	USA	Clinical

94	72	Loss of patched and disruption of granule cell developm ent in a pre-neoplastic stage of medullobl astoma	Oliver, TG	DEVELO PMENT	2005	170	10.63	USA	Basic Science
95	79	Low-stage medullobl astoma: Final analysis of trial comparing standard-dose with reduced-dose neuraxis irradiation	Thomas, PRM	JOURNA L OF CLINICA L ONCOLO GY	2000	170	8.1	USA	Clinical
96	93	AMPLIFI CATION OF THE C-MYC GENE IN HUMAN MEDULL OBLAST OMA CELL-LINES AND XENOGR AFTS	BIGNER, SH	CANCER RESEAR CH	1990	170	5.48	USA	Basic Science

97	74	Medulloblastoma: developmental mechanisms out of control	Marino, S	TRENDS IN MOLECULAR MEDICINE	2005	168	10.5	Switzerland	Review
98	37	BET Bromodomain Inhibition of MYC-Amplified Medulloblastoma	Bandopadhayay, Pratiti	CLINICAL CANCER RESEARCH	2014	167	23.86	USA	Basic Science
99	44	An Animal Model of MYC-Driven Medulloblastoma	Pei, Yanxin	CANCER CELL	2012	167	18.56	USA	Basic Science
100	82	Patched target Igf2 is indispensable for the formation of medulloblastoma and rhabdomyosarcoma	Hahn, H	JOURNAL OF BIOLOGICAL CHEMISTRY	2000	167	7.95	Germany	Basic Science





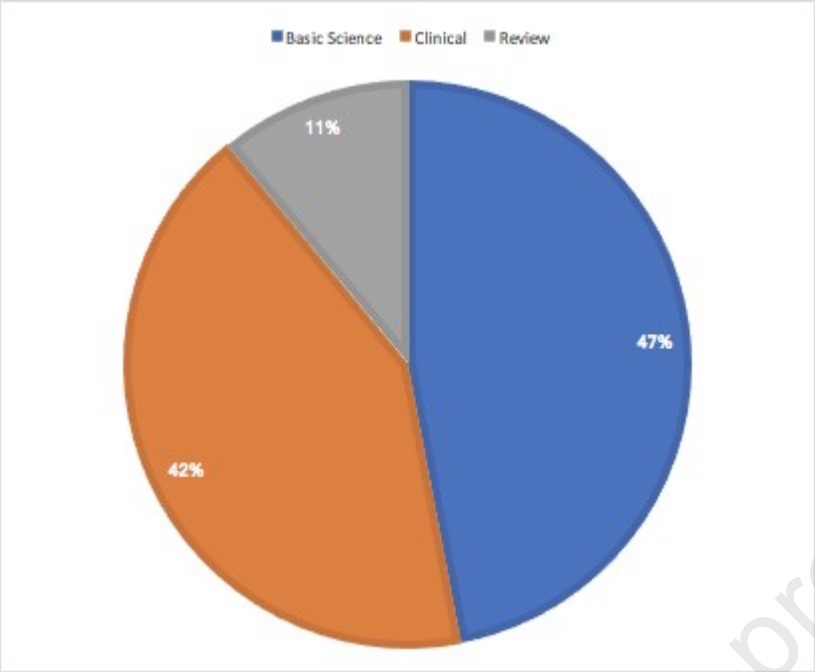


Table 10. List of the studies investigating therapeutics and/or clinical outcomes

Rank by Total Citations	Rank by Average Citations per Year	Title	Authors	Journal Title	Year of Publication	Total Citations	Average Citations per Year
3	3	Brief Report: Treatment of Medulloblastoma with Hedgehog Pathway Inhibitor GDC-0449.	Rudin, Charles M.	NEW ENGLAND JOURNAL OF MEDICINE	2009	727	60.58
8	21	Risk-adapted craniospinal radiotherapy followed by high-dose chemotherapy and stem-cell rescue in children with newly diagnosed medulloblastoma (St Jude Medulloblastoma-96): long-term results from a prospective, multicentre trial	Gajjar, Amar	LANCET ONCOLOGY	2006	500	33.33
10	22	Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma	Packer, Roger J.	JOURNAL OF CLINICAL ONCOLOGY	2006	487	32.47

16	39	Metastasis stage, adjuvant treatment, and residual tumor are prognostic factors for medulloblastoma in children: Conclusions from the Children's Cancer Group 921 randomized phase III study	Zeltzer, PM	JOURNAL OF CLINICAL ONCOLOGY	1999	453	20.59
21	33	Treatment of early childhood medulloblastoma by postoperative chemotherapy alone	Rutkowski, S	NEW ENGLAND JOURNAL OF MEDICINE	2005	447	27.94
24	55	THE TREATMENT OF MEDULLOBLASTOMA - RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL OF RADIATION-THERAPY WITH AND WITHOUT CCNU, VINCRISTINE, AND PREDNISONE	EVANS, AE;	JOURNAL OF NEUROSURGERY	1990	430	13.87
29	85	TREATMENT AND PROGNOSIS OF MEDULLOBLASTOMA IN CHILDREN - A STUDY OF 82 VERIFIED CASES	BLOOM, HJG	AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE	1969	362	6.96

30	98	Medulloblastoma cerebelli - A common type of midcerebellar glioma of childhood	Bailey, P	ARCHIVES OF NEUROLOGY AND PSYCHIATRY	1925	359	3.74
31	59	OUTCOME FOR CHILDREN WITH MEDULLOBLASTOMA TREATED WITH RADIATION AND CISPLATIN, CCNU, AND VINCRISTINE CHEMOTHERAPY	PACKER, RJ	JOURNAL OF NEUROSURGERY	1994	347	12.85
35	50	Intellectual outcome after reduced-dose radiation therapy plus adjuvant chemotherapy for medulloblastoma : A children's cancer group study	Ris, MD	JOURNAL OF CLINICAL ONCOLOGY	2001	323	16.15
36	76	ADJUVANT CHEMOTHERAPY FOR MEDULLOBLASTOMA - THE 1ST MULTICENTER CONTROL TRIAL OF THE INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY (SIOP I)	TAIT, DM	EUROPEAN JOURNAL OF CANCER	1990	321	10.35

41	45	Beta-catenin status predicts a favorable outcome in childhood medulloblastoma: The United Kingdom Children's Cancer Study Group Brain Tumour Committee	Ellison, DW	JOURNAL OF CLINICAL ONCOLOGY	2005	290	18.13
44	58	Postoperative neoadjuvant chemotherapy before radiotherapy as compared to immediate radiotherapy followed by maintenance chemotherapy in the treatment of medulloblastoma in childhood: Results of the German prospective randomized trial HIT '91	Kortman n, RD	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2000	274	13.05
45	68	Neuropsychologic functioning of survivors of childhood medulloblastoma randomized to receive conventional or reduced-dose craniospinal irradiation: A Pediatric Oncology Group Study	Mulhern, RK	JOURNAL OF CLINICAL ONCOLOGY	1998	266	11.57
47	88	MEDULLOBLASTOMA IN CHILDHOOD - SURVIVAL AND FUNCTIONAL RESULTS	HIRSCH , JF	ACTA NEUROCHIRURGICA	1979	254	6.05

48	86	MEDULLOBLASTOMA - CLINICAL PRESENTATION AND MANAGEMENT - EXPERIENCE AT THE HOSPITAL-FOR-SICK-CHILDREN, TORONTO, 1950-1980	PARK, TS	JOURNAL OF NEUROSURGERY	1983	248	6.53
50	65	Patterns of intellectual development among survivors of pediatric medulloblastoma: A longitudinal analysis	Palmer, SL	JOURNAL OF CLINICAL ONCOLOGY	2001	240	12
51	57	Medulloblastoma: signaling a change in treatment	Gilbertson, RJ	LANCET ONCOLOGY	2004	227	13.35
53	53	Neurocognitive consequences of risk-adapted therapy for childhood medulloblastorna	Mulhern, RK	JOURNAL OF CLINICAL ONCOLOGY	2005	226	14.13
57	92	RADIATION TREATMENT FOR MEDULLOBLASTOMA - A 21-YEAR REVIEW	BERRY, MP	JOURNAL OF NEUROSURGERY	1981	221	5.53
56	69	Antitumor activity of the rapamycin analog CCI-779 in human primitive neuroectodermal tumor/medulloblastoma models as single agent and in combination chemotherapy	Geoerger, B	CANCER RESEARCH	2001	221	11.05

58	63	Results of a randomized study of preradiation chemotherapy versus radiotherapy alone for nonmetastatic medulloblastoma: The International Society of Paediatric Oncology United Kingdom Children's Cancer Study Group PNET-3 study	Taylor, RE	JOURNAL OF CLINICAL ONCOLOGY	2003	219	12.17
61	47	Outcome Prediction in Pediatric Medulloblastoma Based on DNA Copy-Number Aberrations of Chromosomes 6q and 17q and the MYC and MYCN Loci	Pfister, Stefan	JOURNAL OF CLINICAL ONCOLOGY	2009	213	17.75
62	95	MEDULLOBLASTOMA - REPORT OF 201 CASES WITH EMPHASIS ON RELATIONSHIP OF HISTOLOGIC VARIANTS TO SURVIVAL	CHATTY, EM	CANCER	1971	213	4.26

63	80	PROSPECTIVE RANDOMIZED TRIAL OF CHEMOTHERAPY GIVEN BEFORE RADIOTHERAPY IN CHILDHOOD MEDULLOBLASTOMA - INTERNATIONAL-SOCIETY-OF-PEDIATRIC-ONCOLOGY (SIOP) AND THE (GERMAN)-SOCIETY-OF-PEDIATRIC-ONCOLOGY (GPO) - SIOP-II	BAILEY, CC	MEDICAL AND PEDIATRIC ONCOLOGY	1995	210	8.08
64	75	Risks of young age for selected neurocognitive deficits in medulloblastoma are associated with white matter loss	Mulhern, RK	JOURNAL OF CLINICAL ONCOLOGY	2001	208	10.4
65	78	Prognostic significance of HER2 and HER4 coexpression in childhood medulloblastoma	Gilbertson, RJ	CANCER RESEARCH	1997	206	8.58
68	66	Clinical, histopathologic, and molecular markers of prognosis: Toward a new disease risk stratification system for medulloblastoma	Gajjar, A	JOURNAL OF CLINICAL ONCOLOGY	2004	199	11.71

69	67	Advantage of protons compared to conventional X-ray or IMRT in the treatment of a pediatric patient with medulloblastoma	St Clair, WH	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2004	198	11.65
78	62	Incidence and severity of postoperative cerebellar mutism syndrome in children with medulloblastoma: a prospective study by the Children's Oncology, Group	Robertson, Patricia L.	JOURNAL OF NEUROSURGERY	2006	186	12.4
79	84	Effects of medulloblastoma resections on outcome in children: A report from the children's cancer group	Albright, AL	NEUROSURGERY	1996	185	7.4
81	87	THE INCIDENCE OF GORLIN SYNDROME IN 173 CONSECUTIVE CASES OF MEDULLOBLASTOMA	EVANS, DGR	BRITISH JOURNAL OF CANCER	1991	184	6.13
86	96	MEDULLOBLASTOMA IN CHILDREN - CORRELATION BETWEEN STAGING AND RESULTS OF TREATMENT	HARISIADIS, L	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	1977	176	4

87	77	Intensity-modulated radiation therapy for pediatric medulloblastoma: Early report on the reduction of ototoxicity	Huang, E	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2002	175	9.21
89	61	Medulloblastoma in childhood: new biological advances	Crawford, John R.	LANCET NEUROLOGY	2007	174	12.43
92	71	Treatment of medulloblastoma with postoperative chemotherapy alone: an SFOP prospective trial in young children	Grill, J	LANCET ONCOLOGY	2005	173	10.81
93	90	IMPROVED SURVIVAL WITH THE USE OF ADJUVANT CHEMOTHERAPY IN THE TREATMENT OF MEDULLOBLASTOMA	PACKER, RJ	JOURNAL OF NEUROSURGERY	1991	172	5.73
95	79	Low-stage medulloblastoma: Final analysis of trial comparing standard-dose with reduced-dose neuraxis irradiation	Thomas, PRM	JOURNAL OF CLINICAL ONCOLOGY	2000	170	8.1

Table 8. List of the studies investigating cellular and molecular biology

Rank by Total Citations	Rank by Average Citations per Year	Title	Authors	Journal Title	Year of Publication	Total Citations	Average Citations per Year
1	6	Altered neural cell fates and medulloblastoma in mouse patched mutants	Goodrich, LV	SCIENCE	1997	1267	52.79
2	1	Molecular subgroups of medulloblastoma: the current consensus	Taylor, Michael D.	ACTA NEUROPATHOLOGICA	2012	785	87.22
5	20	Medulloblastoma growth inhibition by Hedgehog pathway blockade	Berman, DM	SCIENCE	2002	659	34.68
6	8	Smoothened Mutation Confers Resistance to a Hedgehog Pathway Inhibitor in Medulloblastoma	Yauch, Robert L.	SCIENCE	2009	605	50.42
13	16	Targeting brain cancer: advances in the molecular pathology of malignant glioma and medulloblastoma	Huse, Jason T.	NATURE REVIEWS CANCER	2010	462	42
14	64	THE CEREBELLAR MEDULLOBLASTOMA AND ITS RELATIONSHIP TO PRIMITIVE NEUROECTODERMAL TUMORS	RORKE, LB	JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY	1983	458	12.05

23	18	Subtypes of medulloblastoma have distinct developmental origins	Gibson, Paul	NATURE	2010	430	39.09
25	36	Suppression of the Shh pathway using a small molecule inhibitor eliminates medulloblastoma in Ptc1(+/-) p53(-/-) mice	Romer, JT	CANCER CELL	2004	406	23.88
27	25	Medulloblastoma can be initiated by deletion of patched in lineage-restricted progenitors or stem cells	Yang, Zeng-Jie	CANCER CELL	2008	394	30.31
28	30	Acquisition of granule neuron precursor identity is a critical determinant of progenitor cell competence to form Shh-induced medulloblastoma	Schueller, Ulrich	CANCER CELL	2008	365	28.08
32	48	Expression profiling of medulloblastoma: PDGFRA and the RAS/MAPK pathway as therapeutic targets for metastatic disease	MacDonald, TJ	NATURE GENETICS	2001	336	16.8

33	34	PI3K pathway regulates survival of cancer stem cells residing in the perivascular niche following radiation in medulloblastoma in vivo	Hambardzumyan, Dolores	GENES & DEVELOPMENT	2008	332	25.54
34	27	Interfering with Resistance to Smoothened Antagonists by Inhibition of the PI3K Pathway in Medulloblastoma	Buonamici, Silvia	SCIENCE TRANSLATIONAL MEDICINE	2010	328	29.82
37	28	Hedgehog beyond medulloblastoma and basal cell carcinoma	Teglund, Stephan	BIOCHIMICA ET BIOPHYSICA ACTA-REVIEWS ON CANCER	2010	317	28.82
39	56	Atypical teratoid/rhabdoid tumor of the central nervous system: A highly malignant tumor of infancy and childhood frequently mistaken for medulloblastoma - A pediatric oncology group study	Burger, PC	AMERICAN JOURNAL OF SURGICAL PATHOLOGY	1998	307	13.35

42	31	Medulloblastoma: clinicopathological correlates of SHH, WNT, and non-SHH/WNT molecular subgroups	Ellison, David W.	ACTA NEUROPATHOLOGICA	2011	280	28
46	60	Loss of p53 but not ARF accelerates medulloblastoma in mice heterozygous for patched	Wetmore, C	CANCER RESEARCH	2001	257	12.85
49	40	Identification of CD15 as a Marker for Tumor-Propagating Cells in a Mouse Model of Medulloblastoma	Read, Tracy-Ann	CANCER CELL	2009	241	20.08
52	42	MicroRNA profiling in human medulloblastoma	Ferretti, Elisabetta	INTERNATIONAL JOURNAL OF CANCER	2009	226	18.83
55	51	Oxysterols stimulate Sonic hedgehog signal transduction and proliferation of medulloblastoma cells	Corcoran, Ryan B.	PROCEEDINGS OF THE NATIONAL ACADEMY OF	2006	225	15

				SCIENCES OF THE UNITED STATES OF AMERICA			
54	43	Dual and opposing roles of primary cilia in medulloblastoma development	Han, Young-Goo	NATURE MEDICINE	2009	225	18.75
59	23	Enhancer hijacking activates GFI1 family oncogenes in medulloblastoma	Northcott, Paul A.	NATURE	2014	218	31.14
60	46	The miR-17 similar to 92 cluster collaborates with the Sonic Hedgehog pathway in medulloblastoma	Uziel, Tamar	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	2009	215	17.92

66	99	MULTIPLE BASAL-CELL NEVI SYNDROME - AN ANALYSIS OF A SYNDROME CONSISTING OF MULTIPLE NEVOID BASAL-CELL CARCINOMA JAW CYSTS SKELETAL ANOMALIES MEDULLOBLASTOMA AND HYPORESPONSIVENESS TO PARATHORMONE	GORLIN, RJ	CANCER	1965	206	3.68
67	83	EXPRESSION OF THE NEUROTROPHIN RECEPTOR TRKC IS LINKED TO A FAVORABLE OUTCOME IN MEDULLOBLASTOMA	SEGAL, RA	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	1994	201	7.44
70	49	MicroRNA-199b-5p Impairs Cancer Stem Cells through Negative Regulation of HES1 in Medulloblastoma	Garzia, Livia	PLOS ONE	2009	197	16.42
71	54	Daoy medulloblastoma cells that express CD133 are radioresistant relative to CD133- cells, and the CD133+ sector is enlarged by hypoxia	Blazek, Ed R.	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2007	197	14.07
73	38	Rapid, reliable, and reproducible molecular sub-grouping of clinical medulloblastoma samples	Northcott, Paul A.	ACTA NEUROPATHOLOGICA	2012	191	21.22

74	13	Intertumoral Heterogeneity within Medulloblastoma Subgroups	Cavalli, Florence M. G.	CANCER CELL	2017	190	47.5
75	89	A MUSCLE ACETYLCHOLINE-RECEPTOR IS EXPRESSED IN THE HUMAN CEREBELLAR MEDULLOBLASTOMA CELL-LINE TE671	LUTHER, MA	JOURNAL OF NEUROSCIENCE	1989	188	5.88
76	94	ESTABLISHMENT OF A HUMAN MEDULLOBLASTOMA CELL-LINE AND ITS HETEROTRANSPLANTATION INTO NUDE-MICE	JACOBSEN, PF	JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY	1985	188	5.22
83	73	Sonic hedgehog and insulin-like growth factor signaling synergize to induce medulloblastoma formation from nestin-expressing neural progenitors in mice	Rao, G	ONCOGENE	2004	179	10.53
84	100	MEDULLOBLASTOMA + SO-CALLED ARACHNOIDAL CEREBELLAR SARCOMA	RUBINSTEIN, LJ	BRAIN	1964	179	3.14
88	81	Medulloblastoma: clinical and biologic aspects.	Packer, R J	Neuro-oncology	1999	175	7.95

90	97	ESTABLISHMENT OF A HUMAN MEDULLOBLASTOMA CELL LINE	MCALLISTER, RM	INTERNATIONAL JOURNAL OF CANCER	1977	174	3.95
91	41	The clinical implications of medulloblastoma subgroups	Northcott, Paul A.	NATURE REVIEWS NEUROLOGY	2012	173	19.22
94	72	Loss of patched and disruption of granule cell development in a pre-neoplastic stage of medulloblastoma	Oliver, TG	DEVELOPMENT	2005	170	10.63
97	74	Medulloblastoma: developmental mechanisms out of control	Marino, S	TRENDS IN MOLECULAR MEDICINE	2005	168	10.5
98	37	BET Bromodomain Inhibition of MYC-Amplified Medulloblastoma	Bandopadhayay, Pratiti	CLINICAL CANCER RESEARCH	2014	167	23.86
99	44	An Animal Model of MYC-Driven Medulloblastoma	Pei, Yanxin	CANCER CELL	2012	167	18.56

100	82	Patched target Igf2 is indispensable for the formation of medulloblastoma and rhabdomyosarcoma	Hahn, H	JOURNAL OF BIOLOGICAL CHEMISTRY	2000	167	7.95

Table 9. List of the studies investigating genetics

Rank by Total Citations	Rank by Average Citations per Year	Title	Authors	Journal Title	Year of Publication	Total Citations	Average Citations per Year
4	2	Medulloblastoma Comprises Four Distinct Molecular Variants	Northcott, Paul A.	JOURNAL OF CLINICAL ONCOLOGY	2011	700	70
7	29	Mutations in SUFU predispose to medulloblastoma	Taylor, MD	NATURE GENETICS	2002	547	28.79
9	10	The Genetic Landscape of the Childhood Cancer Medulloblastoma	Parsons, D. Williams	SCIENCE	2011	499	49.9
11	4	Dissecting the genomic complexity underlying medulloblastoma	Jones, David T. W.	NATURE	2012	481	53.44
12	5	Molecular subgroups of medulloblastoma: an international meta-analysis of transcriptome, genetic aberrations, and clinical data of WNT, SHH, Group 3, and Group 4 medulloblastomas	Kool, Marcel	ACTA NEUROPATHOLOGICA	2012	477	53
15	7	Novel mutations target distinct subgroups of medulloblastoma	Robinson, Giles	NATURE	2012	456	50.67

17	19	Integrated Genomics Identifies Five Medulloblastoma Subtypes with Distinct Genetic Profiles, Pathway Signatures and Clinicopathological Features	Kool, Marcel	PLOS ONE	2008	452	34.77
18	26	Genornics identifies medulloblastoma subgroups that are enriched for specific genetic alterations	Thompson, MC	JOURNAL OF CLINICAL ONCOLOGY	2006	452	30.13
19	9	Medulloblastoma exome sequencing uncovers subtype-specific somatic mutations	Pugh, Trevor J.	NATURE	2012	451	50.11
20	11	Genome Sequencing of Pediatric Medulloblastoma Links Catastrophic DNA Rearrangements with TP53 Mutations	Rausch, Tobias	CELL	2012	447	49.67
22	12	Subgroup-specific structural variation across 1,000 medulloblastoma genomes	Northcott, Paul A.	NATURE	2012	432	48

26	17	Integrative Genomic Analysis of Medulloblastoma Identifies a Molecular Subgroup That Drives Poor Clinical Outcome	Cho, Yoon-Jae	JOURNAL OF CLINICAL ONCOLOGY	2011	396	39.6
38	15	Genome Sequencing of SHH Medulloblastoma Predicts Genotype-Related Response to Smoothened Inhibition	Kool, Marcel	CANCER CELL	2014	314	44.86
40	35	Multiple recurrent genetic events converge on control of histone lysine methylation in medulloblastoma	Northcott, Paul A.	NATURE GENETICS	2009	298	24.83
43	24	Clonal selection drives genetic divergence of metastatic medulloblastoma	Wu, Xiaocho ng	NATURE	2012	279	31
72	32	Decoding the regulatory landscape of medulloblastoma using DNA methylation sequencing	Hovesta dt, Volker	NATURE	2014	196	28
77	91	STRUCTURAL CHROMOSOMAL-ABNORMALITIES IN HUMAN MEDULLOBLASTOMA	BIGNER, SH	CANCER GENETICS AND CYTOGENETICS	1988	187	5.67
80	52	The origins of medulloblastoma subtypes	Gilbertso n, Richard J.	ANNUAL REVIEW OF PATHOLOGY - MECHANISM	2008	184	14.15

				S OF DISEASE			
82	14	The whole-genome landscape of medulloblastoma subtypes	Northcott, Paul A.	NATURE	2017	180	45
85	70	Genomic and protein expression profiling identifies CDK6 as novel independent prognostic marker in medulloblastoma	Mendrzyk, F	JOURNAL OF CLINICAL ONCOLOGY	2005	176	11
96	93	AMPLIFICATION OF THE C-MYC GENE IN HUMAN MEDULLOBLASTOMA CELL-LINES AND XENOGRAFTS	BIGNER, SH	CANCER RESEARCH	1990	170	5.48

BCNS = basal cell nevus syndrome

CLA = classic

CNS = central nervous system

CY = average citations per year

DN = desmoplastic/nodular

LCA = large cell/anaplastic

MBEN = medulloblastoma with extensive nodularity

PNET = primitive neuroectodermal tumors

PTC = Patched

RS = senior author

SHH = Sonic Hedgehog signaling pathway

SNF = similarity network fusion

SNIP = Source Normalized Impact per Paper

WoS = Web of Science

Table 2. The number of publications per decade for the top 100 most highly cited articles.

Decade	**Number of papers**
1920s	1
1930s	0
1940s	0
1950s	0
1960s	3
1970s	4
1980s	6
1990s	15
2000s	46
2010s	25

Table 3. The frequency of authors who contributed 2 or more articles.

First Author	**Number of Articles**
Northcott, PA	7
Packer, RJ	4
Gilbertson, RJ	3
Kool, M	3
Mulhern, RK	3
Bigner, SH	2
Ellison, DW	2
Gajjar, A	2
Taylor, MD	2

Table 4. The journal of publications in which the top 100 most cited articles were published.

Rank	Journal of Publication	Number of articles (n=100)	Source-normalized impact per paper (SNIP)	SCImago journal rank
1	Journal of Clinical Oncology	16	5.22	11.754
2	Nature	9	9.20	16.345
3	Cancer Cell	7	4.57	11.741
4	Journal of Neurosurgery	6	2.00	1.69
5	International Journal of Radiation Oncology, Biology, Physics	5	1.72	2.29
6	Acta Neuropathologica	4	4.08	8.34
6	Cancer Research	4	1.60	4.05
6	Science	4	7.31	13.25
7	Lancet Oncology	3	9.24	18.07
7	Nature Genetics	3	5.48	21.51
7	Proceedings of the National Academy of Sciences of the United States of America	3	2.54	5.6
8	International Journal of Cancer	2	2.39	3.28
8	Journal of Neuropathology	2	0.89	1.67

	and Experimental Neurology			
8	New England Journal of Medicine	2	13.00	19.524
8	Cancer	2	2.03	3.49
8	PLOS One	2	1.12	1.1
N/A	Other*	26	N/A	N/A

*Journals with only one article each predominated the top 100 list

Table 5. Countries of origin for the top cited papers on medulloblastoma.

Country of origin	**Number of Articles**
USA	63
Germany	12
Canada	10
England	6
Australia	2
Italy	2
Austria	1
France	1
Netherlands	1
Sweden	1
Switzerland	1

Table 6. Top contributing institutions based on first author*

Institution	**Country**	**Number of Articles**
St. Jude Children's Research Hospital	USA	14
University of Toronto/Hospital for Sick Children	Canada	9
German Cancer Research Center	Germany	8
Children's National Hospital	USA	5
Johns Hopkins	USA	4
Children's Hospital of Philadelphia (UPenn)	USA	4
Harvard Medical School/Massachusetts General Hospital/Boston Children's Hospital	USA	4
Duke University Medical Center	USA	4
Stanford University	USA	3

*Institutions with 3 or more articles were included

Table 7. Category type of the 100 most cited articles.

Article Category	**Number of Articles**
Basic Science	47
Clinical	42
Review	11

Declaration of interests

All authors (Nolan J. Brown, Bayard Wilson, Anushka Paladugu, Shane Shahrestani, Brian V. Lien, Katelynn Tran, Seth C. Ransom, Ali Tafreshi, Ryan C. Ransom, Alvin Chan, Isaac Yang, Elliot Choi, and Ronald Sahyouni) declare to the following below: They have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.