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Multi-omics convergence in odontogenic neoplasm research: a scientometric and translational mapping study

Convergência de multiômica na pesquisa de neoplasias odontogênicas: um estudo cienciométrico e de mapeamento translacional

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ABSTRACT

Background: Odontogenic tumors (OTs), though rare, pose diagnostic and therapeutic uncertainties due to their heterogeneous behavior. With the advancement of omics technologies like genomics, transcriptomics, proteomics, and metabolomics, molecular understanding of OTs has expanded rapidly. **Objective:** The aim of this bibliometric analysis is to map literature on omics-driven OT research and evaluate its translational potential in diagnostics, biomarker discovery, and targeted therapy. **Material and Methods:** A bibliometric analysis of peer-reviewed OT-related omics literature from Scopus databases (until June 2025) was conducted. Tools such as Bibliometrix (R) and VOSviewer were used for network visualization, thematic evolution mapping, and hub gene identification, respectively. **Results:** Omics-based OT research showed exponential growth post-2010, with transcriptomics leading in recent years. Keyword and thematic analysis revealed an evolution from basic gene discovery to pathway-targeted translational research. Further, bibliometric analysis highlighted important biomarkers such as podoplanin, Cripto-1, and BCL-2 in OTs diagnosis. **Conclusion:** Multi-omics research in odontogenic tumors (OTs) has shown significant insights for diagnosis and treatment. Advancing this field will require strong cross-disciplinary collaboration and reliable validation methods. Despite the seriousness of OTs, omics-based research in this area is still in its early stages showing there's a real need and opportunity for more focused and sustained efforts.

KEYWORDS

Bibliometric analysis; Genetic disease; Multi-omics; Neoplasm; Odontogenic tumors.

RESUMO

Contexto: Tumores odontogênicos (TO), embora raros, apresentam incertezas diagnósticas e terapêuticas devido ao seu comportamento heterogêneo. Com o avanço das tecnologias ômicas como a genômica, transcriptômica, proteômica, e metabolômica, a compreensão molecular de TO expandiu rapidamente. **Objetivo:** O objetivo desta análise bibliométrica é mapear a literatura sobre pesquisa em TO impulsionada por abordagens ômicas e avaliar seu potencial translacional em diagnósticos, descoberta de biomarcadores e terapia direcionada. **Material e Métodos:** Uma análise bibliométrica de literatura ômica relacionada a TO revisada em pares da base de dados Scopus (até Junho de 2025) foi conduzida. Ferramentas como *Bibliomatrix* (R) e *VOSviewer* foram empregadas para visualização de rede, mapeamento de evolução temática, e identificação de genes centrais, respectivamente. **Resultados:** Pesquisas ômicas de TO mostraram um crescimento exponencial após 2010, com predominância de transcriptômica nos últimos anos. Análise de palavras-chave e temática revelou uma evolução desde a descoberta gênica básica até a pesquisa translacional direcionada a vias de sinalização. Em adendo, a análise bibliométrica destacou biomarcadores importantes como a podoplanina, Cripto-1,e BCL-2 no diagnóstico de TO. **Conclusão:** A pesquisa multiômica em TO tem mostrado insights significativos para o diagnóstico e tratamento. Avanços nesta área vão requerer uma colaboração transdisciplinar forte e métodos de validação confiáveis. Apesar da gravidade dos TO, a pesquisa ômica nesta área ainda está em estágios iniciais, demonstrando que há uma necessidade real e oportunidade para esforços mais focados e sustentados.

PALAVRAS-CHAVE

Bibliometria; Doença genética; Multiômica; Neoplasias; Tumores odontogênicos.

INTRODUCTION

Odontogenic tumors (OTs) are a diverse group of neoplasms originating from dental lamina, including odontogenic epithelium, ectomesenchyme, mixed or remnants of the odontogenic apparatus [1,2]. OT exhibit a broad spectrum of clinical behaviors ranging from hamartomas like odontomas to locally aggressive tumors such as ameloblastomas [3]. The World Health Organisation (WHO) categories these tumors into epithelial, mesenchymal, and mixed odontogenic tumors [4]. Benign variants such as ameloblastoma, adenomatoid odontogenic tumor (AOT), and odontomas are more frequently encountered, while malignant forms like ameloblastic carcinoma and odontogenic sarcoma are extremely rare [5,6]. These tumors can occur in a wide age range and more commonly in the jaws, with site predilection varying across types [7]. The clinical manifestations of odontogenic tumors are often non-specific, from asymptomatic radiographic findings to progressive swelling, facial asymmetry, and displacement of teeth [8]. Few lesions grow silently over years, while others present rapidly with cortical expansion or even perforation [9]. Radiographically, these tumors may appear as unilocular or multilocular radiolucencies, occasionally with calcifications or tooth-like structures, complicating differentiation from cystic lesions [10]. Histopathological examination remains the gold standard for diagnosis, although overlapping morphological features between various entities can pose challenges. Accurate diagnosis is essential for appropriate surgical planning, as treatment varies from conservative enucleation to radical resection. Furthermore, high recurrence rates in certain tumors like multicystic ameloblastoma necessitate long-term follow-up.

In recent decades, omics technologies have revolutionised biomedical research [10,11]. Genomics has enabled mutation profiling; transcriptomics reveal differential gene expression; proteomics highlights protein-level deregulation; and metabolomics reflects downstream metabolic shifts [12]. Applying these technologies to understand the initiation, pathogenesis and progression in odontogenic tumors has the potential to decode the molecular landscape in pathogenesis, progression, and response to therapy [13].

Their application in oncology has revolutionized biomarker discovery, tumor classification, and therapy prediction, but odontogenic tumor research has been comparatively slow in adopting these tools. Although there are limited studies that have explored *BRAF* (v-Raf murine sarcoma viral oncogene homolog B1) mutations in ameloblastomas [14] and *PTCHI (*Patched-1 gene) in keratocystic lesions [15], yet multi-omics studies remain scarce. Given the complexity and varied behavior of these tumors, multi-omics convergence has the potential to redefine diagnostic criteria, unveil molecular subtypes, and identify targets for individualized therapy, thereby advancing precision oral pathology.

Bibliometric and scientometric analysis are quantitative research methodology that enable systematic evaluation of scientific literature using metrics such as publication volume, citation trends, authorship networks, and keyword dynamics [16]. It plays a vital role in mapping research evolution, identifying gaps in knowledge, and guiding future investigations. Even though bibliometric studies have been widely employed in fields such as oncology and precision medicine, their application in OT research remains unexplored [10]. Prior studies in oral squamous cell carcinoma (OSCC) have successfully used bibliometrics to uncover emerging molecular targets, collaborative networks, and thematic shifts, contributing significantly to the understanding of diagnostic and prognostic markers [17]. Implementing a similar approach to OTs can provide the research landscape, especially considering the fragmented and underrepresented nature of omics studies in this domain. Recent advancements highlight the growing use of omics in odontogenic tumor research, including laser capture microdissection for precise molecular profiling, proteomic studies revealing differential protein expression in fibro-osseous lesions and ameloblastoma, and genomic analyses identifying BRAF-V600E–associated metabolic alterations [18-20]. By mapping the multi-omics technologies in OT research, bibliometric analysis will help delineate knowledge clusters, highlight translational trends, and identify opportunities for interdisciplinary collaboration thereby supporting the development of precision diagnostic frameworks in oral pathology.

METHODS

The bibliometric analysis was designed to explore how omics-based research has evolved within the field of odontogenic tumors.

A structured literature search was performed on July 4, 2025, covering all publications indexed in Scopus up to that date. The search strategy was carefully formulated using relevant terms linked to both odontogenic tumors (e.g., "ameloblastoma," "odontoma," "adenomatoid odontogenic tumour," "keratocystic odontogenic tumour") and omics technologies (e.g., "genomics," "proteomics," "transcriptomics," "metabolomics," "multi-omics"). The aim was to capture all potentially relevant studies or literature without imposing any document-type filters or exclusion criteria, so that the landscape could be assessed in its entirety (Figure 1).

The full bibliographic data set comprising article titles, author names, institutional affiliations, countries, keywords, source journals, and citation information was exported in Excel format for analysis. We used a combination of established bibliometric tools for processing and visualization: Bibliometrix [21] (RStudio environment) for core statistics, annual growth, thematic evolution, and source dynamics; VOSviewer [22] for mapping co-authorship, institutional collaboration, word clouds, heatmap and keyword clustering signal within the Scopus data set. This approach enabled us to gain an unbiased, descriptive understanding of how

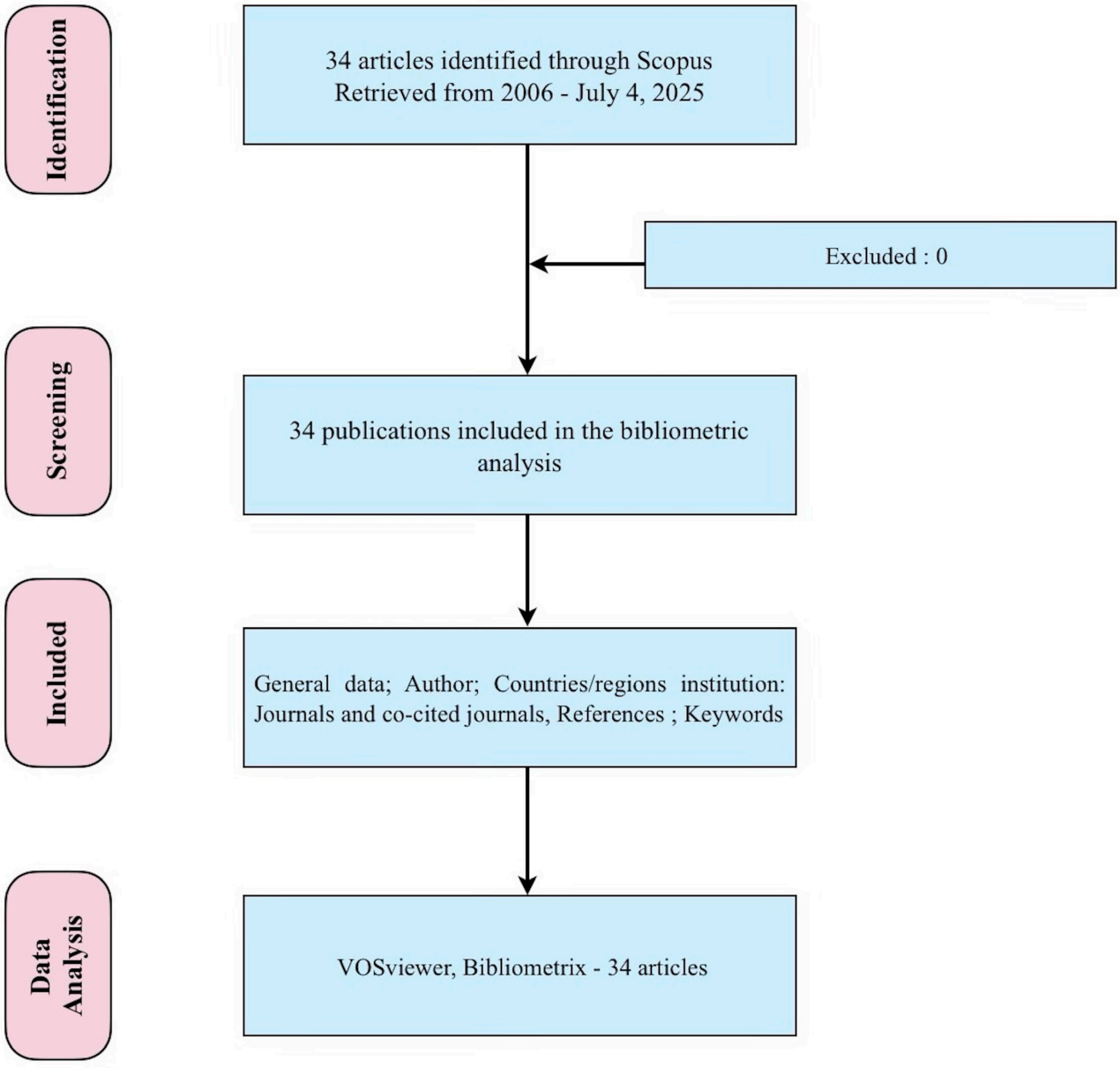

Figure 1 - Flow chart of search strategy.

multi-omics research is emerging in the context of odontogenic tumors.

RESULTS

Overview

The bibliometric data set comprises 34 documents published between 2006 [23] and 2025 [9] representing contributions from 229 authors across 27 distinct journals. The literature on OT shows a moderate annual growth rate of 5.95%, with an average document age of 4.59 years, which point to the current and evolving nature of the theme. The average citation per document is 15.68, denoting a moderate impact per article. The papers were multi-authored (Number of Authors per document 7.79) highlighting a highly collaborative research area. Further, the international collaboration index stands at 35.29%, suggesting substantial global research exchange in the field of OT, particularly in the context of multiomics and molecular diagnostics area (Figure 2). Bibliometric mapping of the included studies, particularly keyword co-occurrence and frequency analysis, identified podoplanin, Cripto-1, and BCL-2 as the most consistently explored biomarkers in odontogenic tumor diagnostics. This observation fits within the broader biomarker landscape across odontogenic tumors, which spans three interconnected molecular domains: signaling regulators, extracellular-matrix components, and genomic alterations. Cell-cycle and survival markers such as podoplanin, BCL-2, p53, and HIF-1α illustrate the proliferative and hypoxia-adaptive behavior characteristic of KCOT/OKC and ameloblastoma, while ECM-related proteins including multiple collagen isoforms, annexins, desmosomal components, and odontogenic matrix molecules underscore the central role of tumor–stroma interactions in primordial OT biology. Complementing these patterns, recurrent genetic drivers such as BRAF-V600E, PTCH1, SMO, and CTNNB1 map the evolutionary trajectory of these lesions, supporting the view that odontogenic tumors arise from a coordinated network of structural, metabolic, and oncogenic pathways rather than isolated molecular events (Table I).

Annual scientific production

The yearly scientific output reveals a distinct upward trend, with sparse publications in the early phase (2006-2014) and a marked increase post-2018. The highest number of publications were seen between 2022 [5] and 2023 [24], each with six papers each year, indicating that multiomics and molecular-based studies in OTs have gained considerable traction in the past five years. This surge may reflect growing interest in translational approaches integrating genomics, transcriptomics, and proteomics in head and neck pathology. The exponential rise in papers suggests the field is moving from an exploratory phase into a more evidence-generating, data-driven domain (Figure 3).

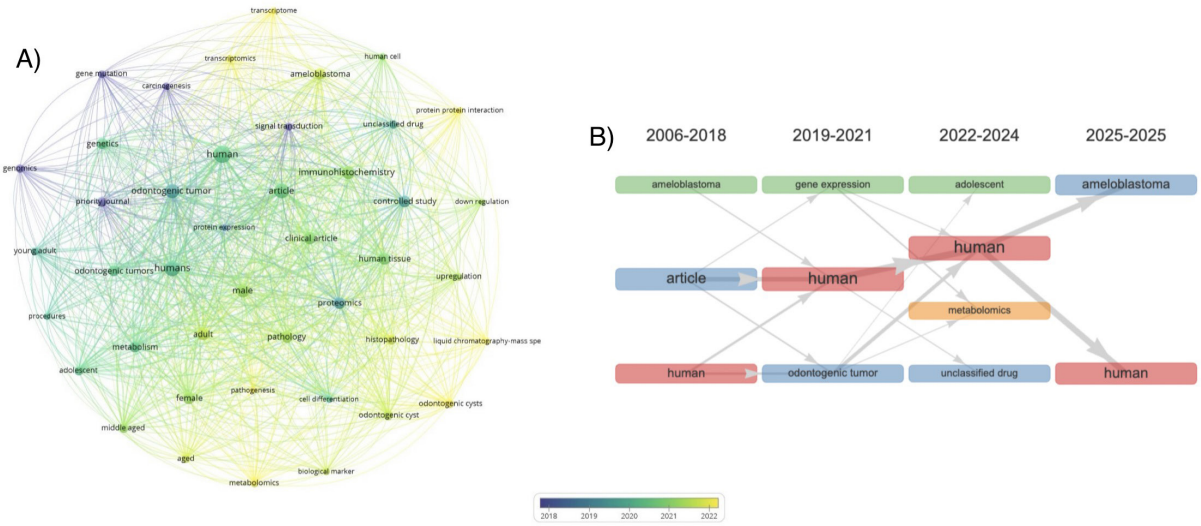

Figure 2 - Keyword Cloud (A) Network visualization showing keyword co-occurrence clusters where node size denotes frequency of occurrence and color indicates thematic grouping; (B) Timeline of trending topics (2006-2025); green: genetic/developmental, red:human studies, blue: clinical/pathological, orange: analytical approaches.

Table I - Biomarker Profile of Odontogenic Tumours

Biomarker	Functional Role	Odontogenic Tumour Context	No. of Studies
Podoplanin	Cell motility, invasion	Expressed in odontomas and ameloblastic fibro-odontomas; linked to epithelial–mesenchymal transition	1
Cripto-1	Oncogenic signaling, TGF-β modulation	Proposed diagnostic/molecular biomarker in OT classification	1
BCL-2	Anti-apoptotic regulator	Overexpressed in KCOT/OKC and BCNS-associated OKCs	1
Cyclin D1	Cell-cycle progression	Frequently upregulated in KCOT/OKCs	1
CD56	Cell adhesion / neural cell adhesion molecule	Reported in KCOT/OKC epithelial layers	1
CK18	Cytokeratin subtype	Altered epithelial differentiation marker in OKC	1
p53	Tumour suppressor	Increased expression in KCOT/OKC and ameloblastoma hypoxia-related pathways	2
PCNA	Proliferation index	High proliferative activity in KCOT/OKCs compared to cysts	1
IAP-2	Anti-apoptotic protein	Linked to ameloblastoma resistance under hypoxia	1
HIF-1α	Hypoxia response regulator	Associated with survival in hypoxic ameloblastoma microenvironment	1
COL1A1 / COL1A2	Collagen synthesis, ECM integrity	Highly expressed in KCOT/OKC proteomic studies; expressed in POT tumorigenesis	3
COL6A1 / COL6A2 / COL6A3	ECM organization, stromal modulation	Found in both BOL-derived EVs and KCOT/OKC proteomics	2
COL12A1 / COL14A1	ECM structural regulation	Reported as KCOT/OKC specific proteins	1
ACTB (β-actin)	Cytoskeletal protein	Detected in EV-based proteomic profiling of benign odontogenic lesions	1
ANXA2 / ANXA4 / ANXA5 / ANXA6	Annexins involved in membrane trafficking	Highly expressed in KCOT/OKC vs radicular cysts	1
FBN1	ECM glycoprotein	Identified in EV-derived vesicle proteomics	1
DSPP, DMP1, AMELX, AMBN, ENAM	Odontogenic matrix proteins	Expressed in primordial odontogenic tumor pathways; reflect developmental signaling	1
Desmosomal proteins (plakoglobin, plakophilin-1, desmoglein-3, desmoplakin)	Cell-cell adhesion	Deregulated in KCOT/OKC vs radicular cysts	2
MAPK12	Stress-activated kinase	Upregulated in KCOT/OKC proteomic profiles	1
AIDA	Annexin-associated protein	Proposed novel biomarker candidate for KCOT/OKC	1
CDH3 (P-cadherin)	Adhesion molecule	Upregulated in ameloblastoma proteomics	1
BRAF-V600E	MAPK pathway activation	Strong driver mutation in ameloblastoma; metabolic shift demonstrated	3
SMO	Hedgehog pathway	Detected in ameloblastomas; linked to genomic instability	1
PTCH1	Hedgehog receptor	Altered in NBCCS-related jaw lesions; regulates SPARC expression	1
FGFR2 / PIK3CA / EGFR / ROS1	Multiple oncogenic signaling	Detected in targeted sequencing of complex ameloblastomas	1
CDC73	Tumour suppressor gene	Somatic mutations in cemento-ossifying fibroma	1
CTNNB1	Wnt signaling	Altered in ghost cell odontogenic carcinoma	1
MAP3K, EP300	Regulatory genes	Reported as novel alterations in GCOC	1

Average citations per year

While overall citation metrics are moderate, the highest citation averages are attributed to articles from 2006 [23] and 2014 [25], which garnered 19 and 14.95 citations per article, respectively. These preceding papers seem to be pivotal and have had sufficient time to build impact. On the other hand, papers from 2022 [26] onwards seem to lack citations, which may be due to the publication date rather than quality or relevance. This trend emphasizes the role of citation latency in bibliometric measurements, especially in new areas of research where important insights and discoveries are shared in the final years but have not been adopted in practice by the clinical or research community (Figure 3).

Three-field plot (cited references-authors-keywords)

The three-field plot analysis revealed that the most frequently cited references are strongly associated with a few prominent authors which include Gomez et al. [7] and Diniz et al. [8], who dominate the literature landscape in this domain. Their studies on OT frequently intersect with keywords such as "odontogenic tumours," "immunohistochemistry," "gene expression," and "clinical article," indicating a molecular pathology-oriented focus. The overlap of cited references and author contributions with thematic keywords suggests a high degree of specialization and a tightly interconnected research niche, predominantly centered around histomolecular characterization and diagnostic innovation in odontogenic tumors (Figure 4).

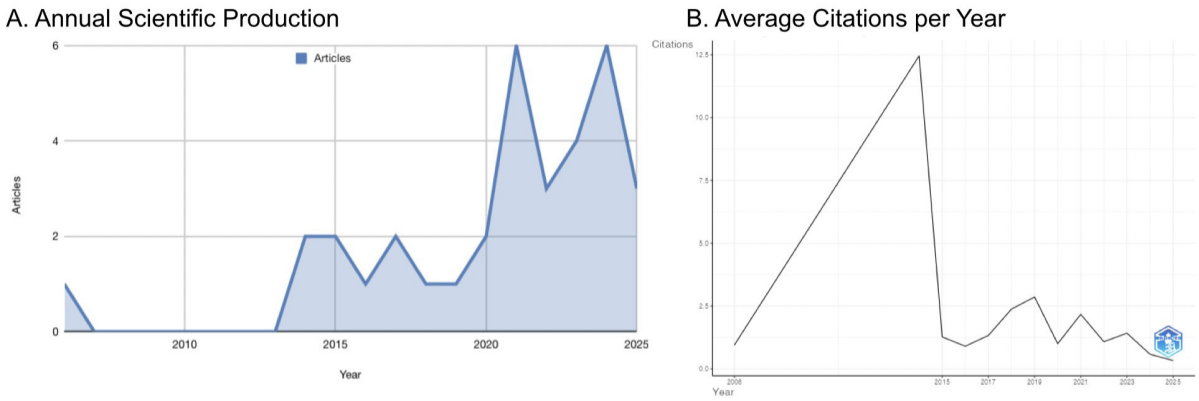

Figure 3 - (A) Annual scientific production of omics-based odontogenic tumor research from 2006-2025; (B) Year-wise average citations per article reflecting the temporal citation impact across the field.

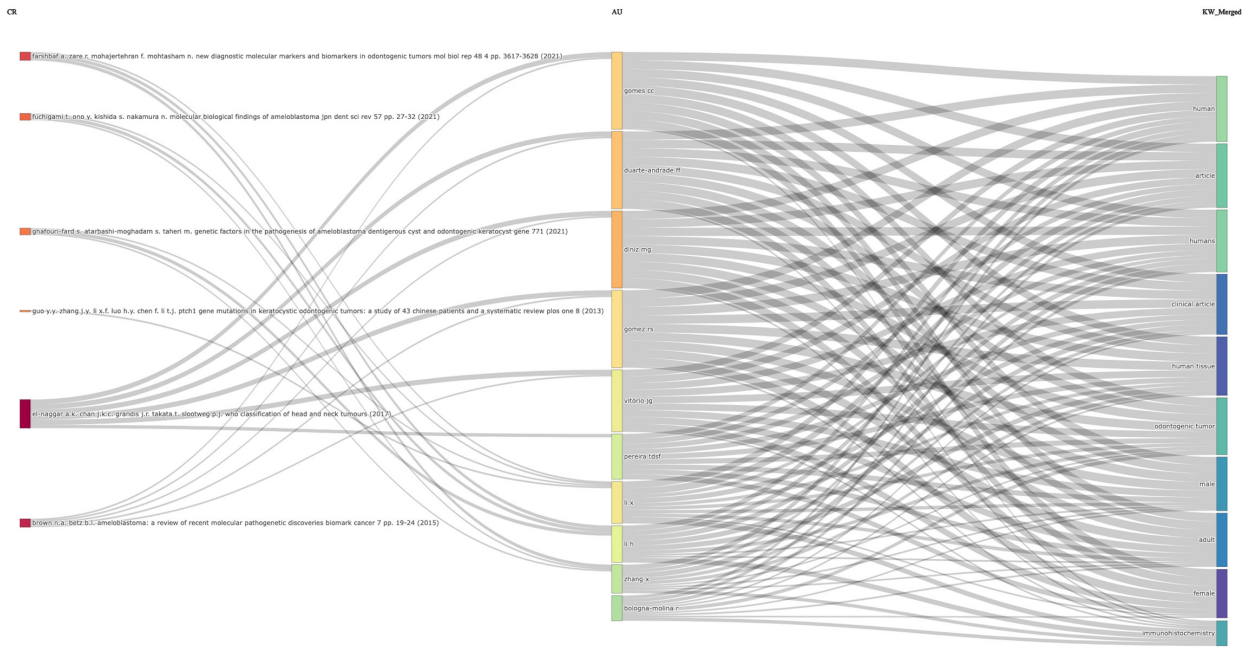

Figure 4 - Three-field plot visualizing the intersection between cited references, contributing authors, and keywords.

Most relevant sources

Journal of Oral Pathology & Medicine [13,19,20,27] and Oral Diseases [8,18,26,28] were the most prominent journals, each contributing four articles, followed by Oral Oncology. These journals consistently publish high-quality studies on diagnostic pathology and molecular markers relevant to OT. Further, these journals have served as key platforms for interdisciplinary research dissemination. The concentration of publications in these specialty journals indicates that this niche research area is sustained by dedicated sections within oral and maxillofacial pathology, which are increasingly receptive to multiomics and computational approaches (Figure 5).

Bradford's law (core journals)

Bradford's Law yielded a three-zone distribution, with five core journals in Zone 1, including Journal of Oral Pathology & Medicine [13,19,20,27], Oral Diseases [8,18,26,28], Oral Oncology [29], Biomedical Reports [30], and BMC Oral Health [20]. These journals collectively contain the most influential and frequently cited articles in literature The remaining journals in Zones 2 and 3 are more dispersed and reflect peripheral or interdisciplinary contributions. The presence of bioinformatics and clinical translational journals within the core zone signifies the increasing convergence of molecular science with clinical diagnostics in the study of odontogenic tumors (Figure 6).

Local impact by source (h-index)

Analysis of local h-index across sources revealed that both Journal of Oral Pathology & Medicine [13,19,20,27] and Oral Diseases [8,18,26,28] held an h-index of 4, indicating that at least four of their articles have been cited four or more times within the data set. This shows how relevant and scientifically visible they are in the field.

Other journals, on the other hand, have lower H-indices, which could mean that they are new to the field or have less influence. The fact that these high h-index journals are so popular shows that they are important not only for the number of publications they produce but also for how they shape the direction of research through citation impact and academic recognition (Figure 7).

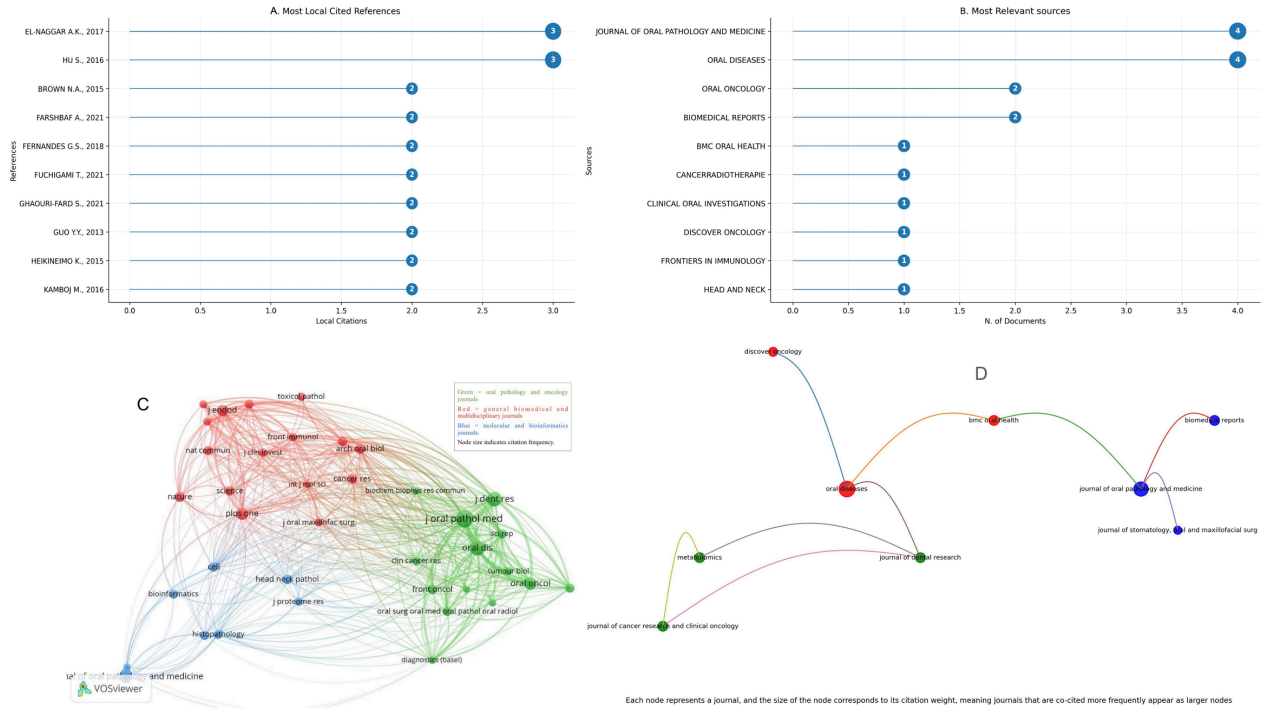

Figure 5 - (A) Distribution of publications across journals, with node size representing the number of publications and positioned proportionally to publication frequency; (B) Journal co-citation network where node size indicates citation frequency and color denotes distinct thematic clusters of journals within the field; (C) Bibliographic coupling of journals illustrating shared references, where node size reflects citation strength and color differentiates related research domains; (D) Most cited authors' network, where node size represents total citation count and the connecting lines indicate co-citation relationships among key contributors.

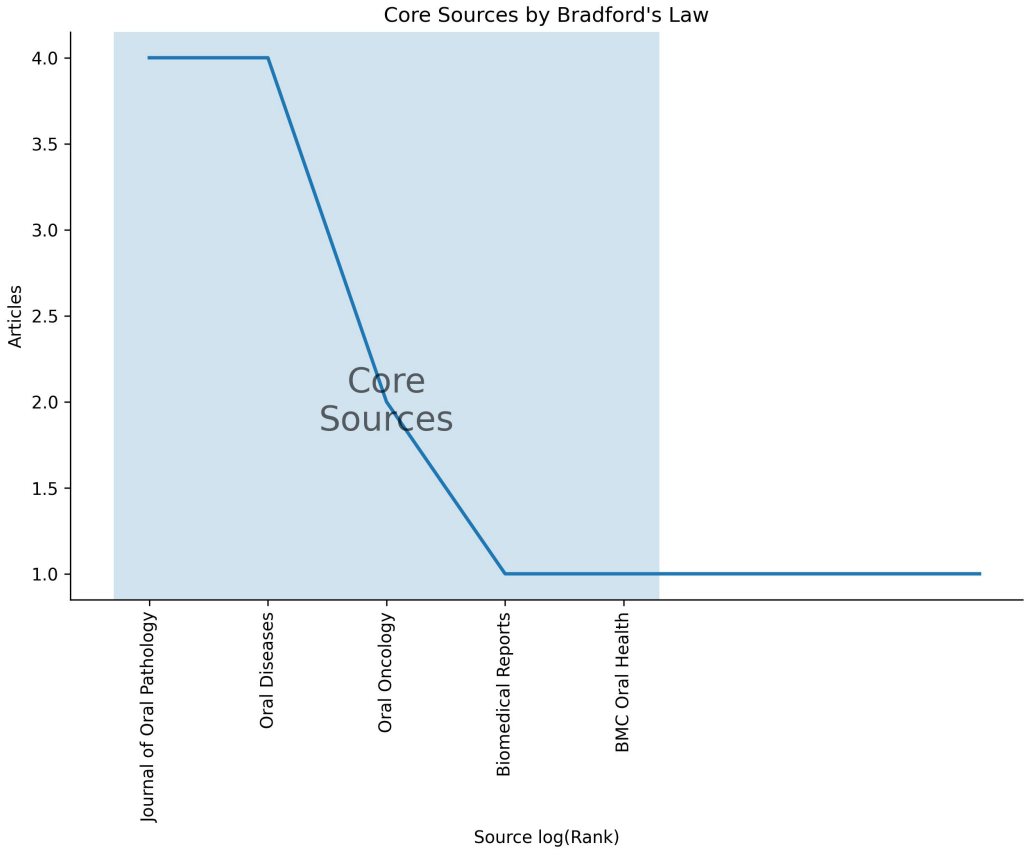

Figure 6 - Bradford's Law application delineating core, middle, and peripheral journal zones.

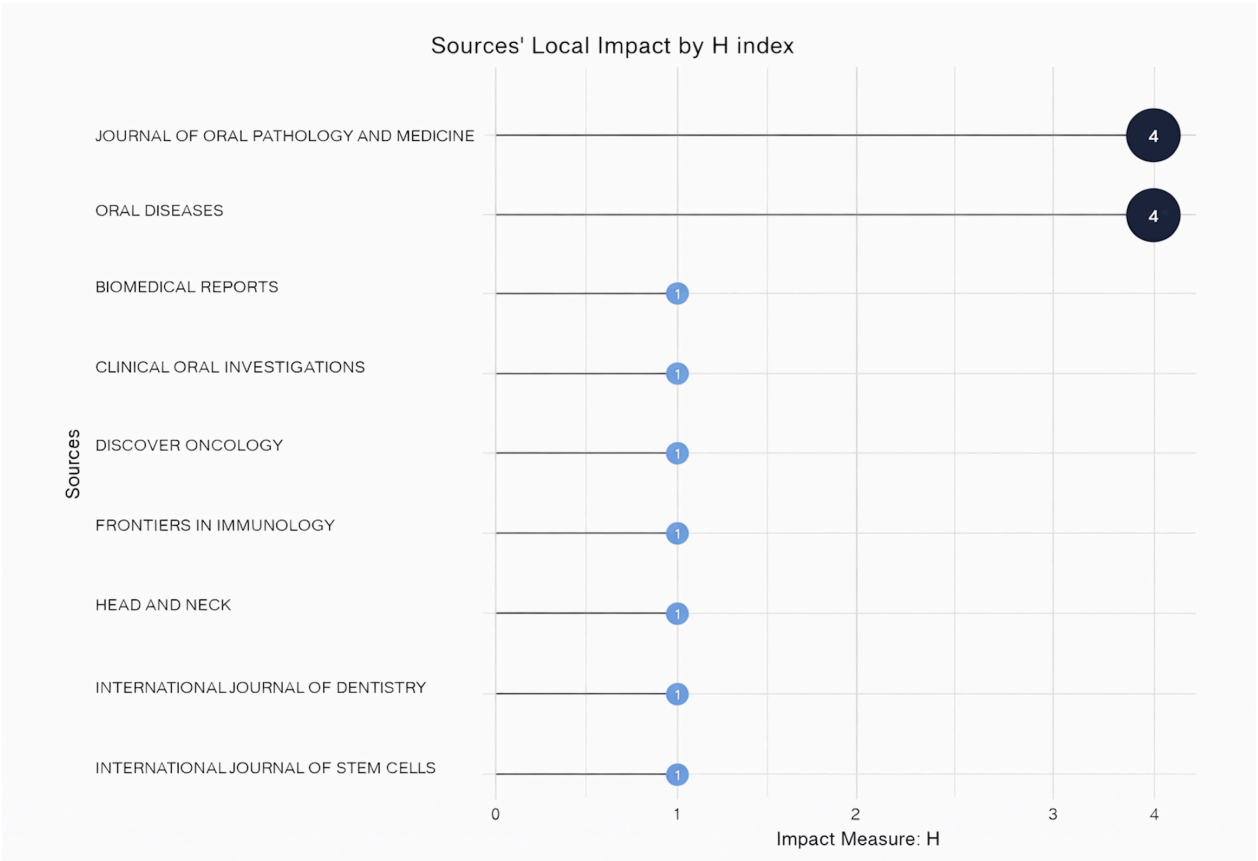

Figure 7 - Local citation impact of journals measured through h-index within the data set.

Source growth over time

Core journals include the Journal of Oral Pathology & Medicine [13,19,20,27] and Oral Diseases [8,18,26,28] who have consistently published papers over the years. Newer sources, primarily published after 2020, include Clinical Oral Investigations [10], Frontiers in Immunology [31], and Discover Oncology [32]. This change corresponds with the growing use of systems biology and omics-based methods in diagnostic oral pathology and represents an expansion into more extensive biomedical and immunological domains. A growing interdisciplinary interest in tumor biology and the translational significance of odontogenic neoplasms may also be indicated by this diversification (Figure 8).

Most relevant authors

The most productive authors include Diniz MG and Gomes CC (5 papers each), followed by Gomez RS (4 papers) and Duarte-Andrade FF (3 papers) [7,8,10,11]. These authors appear often in multiple analysis fields, citations, co-authorship networks, and keyword associations. This work often involves genetic and molecular profiling, supporting the current shift toward multi omics-based classification and risk stratification models for odontogenic tumors. Their consistent presence suggests the existence of a focused research hub or consortium that could be further mapped using co-authorship or citation network analysis (Figure 9).

Geographical analysis

Geographical analysis of omics-based research in odontogenic tumors revealed distinct regional patterns, with Brazil leading in publication output (74 articles), followed by China (52) and the United States (39). Despite lower publication volume, the US recorded the highest total citations (338) and average citations per article (67.6), indicating strong global impact. Japan and Iran also demonstrated comparatively high citation rates, whereas India and China, though productive, had modest citation impact. Temporal trends highlighted a sharp rise in Brazil's output post-2019, and consistent growth from China and Japan after 2016. Collaborative analysis showed largely regional partnerships, with Brazil linking to Canada, Mexico, and South Africa, and the US collaborating with Japan

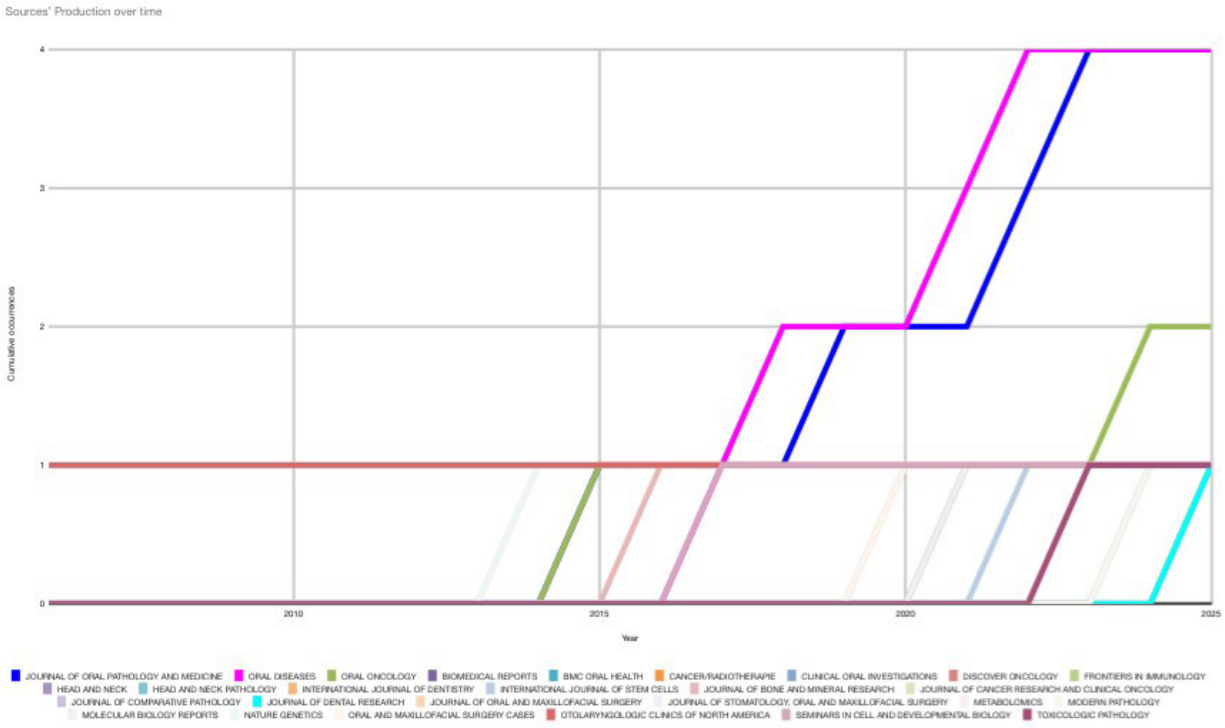

Figure 8 - Temporal trend of source productivity showing cumulative publication occurrences per year, with each colored line representing a distinct journal's contribution to the field over time.

and the UK, yet no dominant global research networks were observed. This underscores a growing but fragmented global landscape, where scientific productivity is expanding, but high-impact, cross-national synergy remains limited (Figure 10 and 11).

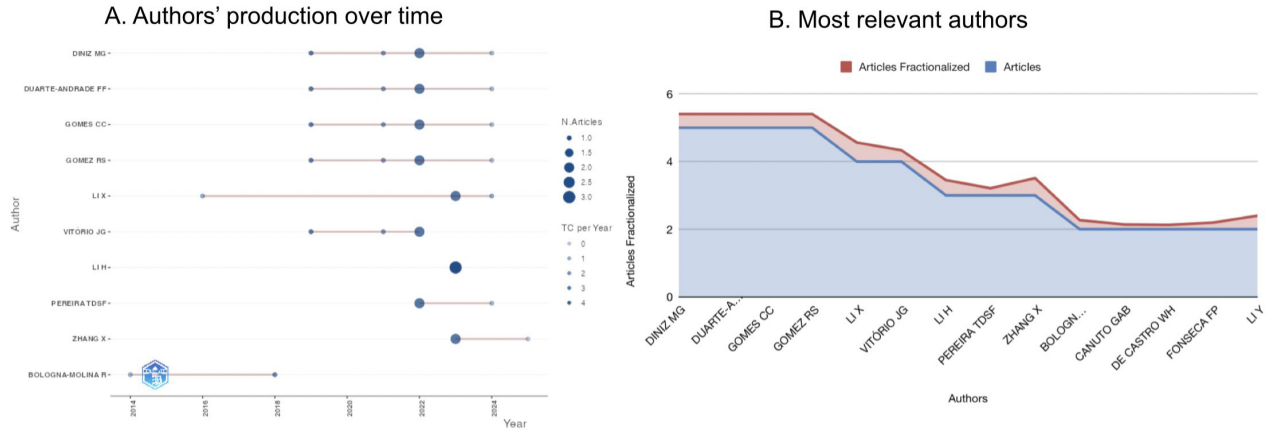

Figure 9 - (A) Most relevant authors; (B) Authors' production over time.

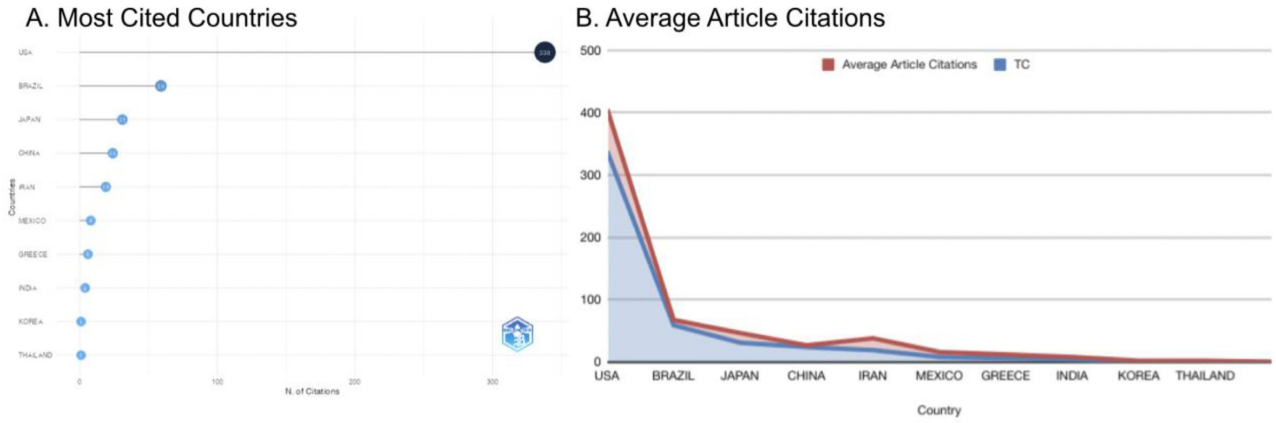

Figure 10 - (A) Most cited documents globally; (B) Average article citations.

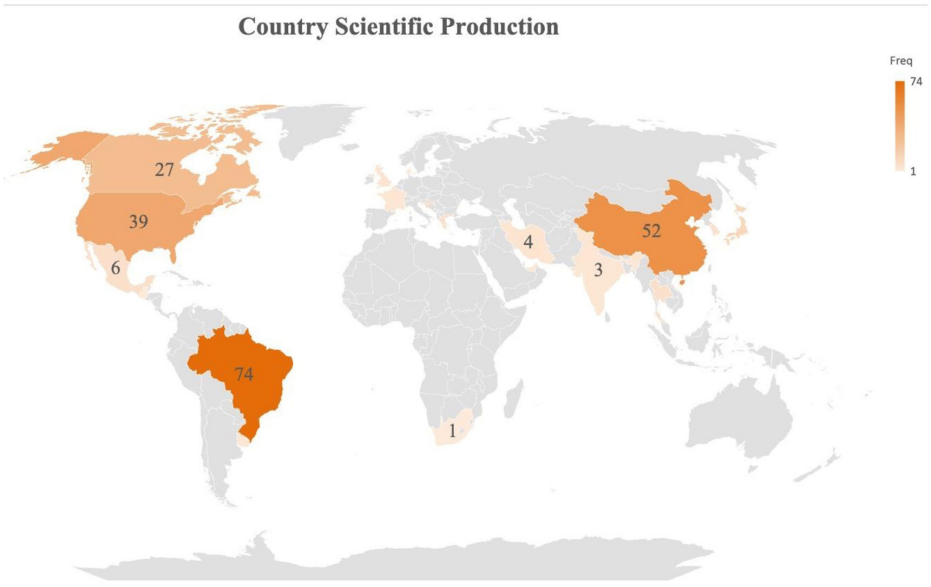

Figure 11 - Geographical Distribution of OT Omics Research.

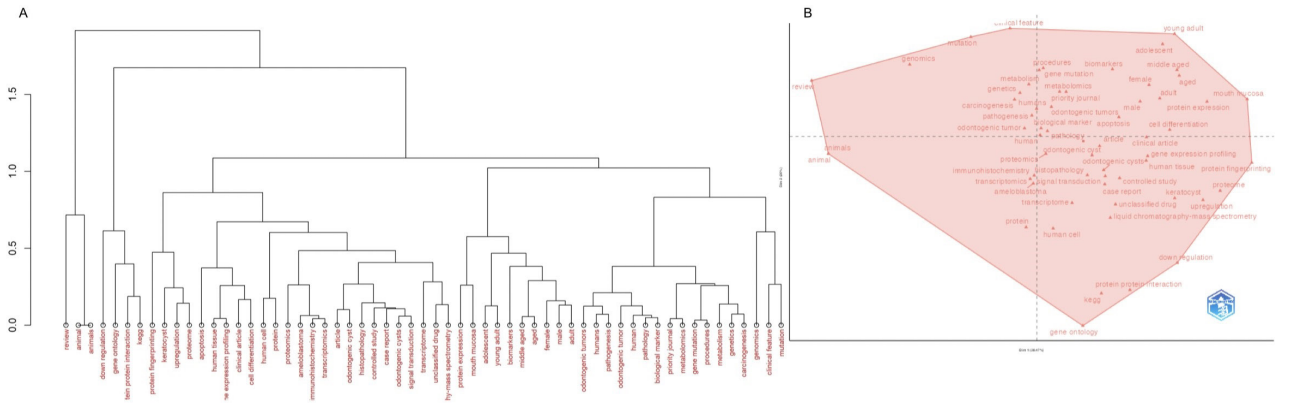

Figure 12 - (A) Hierarchical clustering dendrogram; (B) Factorial map representing the conceptual structure of the literature based on keyword co-occurrence.

Factorial analysis

Factorial analysis revealed two principal conceptual dimensions in the literature on odontogenic tumors: one aligned with traditional clinical and histopathological parameters (e.g., "ameloblastoma," "histopathology," "odontogenic cyst"), and the other representing an emerging cluster of molecular and omics-driven terms (e.g., "transcriptome," "gene ontology," "proteomics"). The distribution across these axes indicates a conceptual polarity between foundational descriptive frameworks and advanced systems biology approaches. Hierarchical clustering further supported this distinction, showing dense co-occurrence among keywords like "gene mutation," "signal transduction," and "protein interaction," suggesting a growing convergence of molecular biology and translational oral pathology in OT research (Figure 12).

DISCUSSION

The application of multi-omics approaches in tumor research has grown exponentially across various medical disciplines, yet odontogenic tumors (OTs) remain relatively underrepresented in this paradigm. Though these tumors are uncommon, their complex clinical presentation and diverse histological features necessitate further molecular studies [33]. As our bibliometric results indicate, there is still expansive work to be done utilizing omics in OTs, especially with more focus on the subclasses such as ameloblastoma and keratocystic odontogenic tumors. Insights from genomic studies, such as *BRAF* and *PTCH I* mutations, have emerged as points of focus, but there is a lack of integration with transcriptomic, proteomic, or metabolomic data. This shows that although some omics-based studies are being conducted, multi-layered, comprehensive frameworks are still at their preliminary stages of development.

The collaboration network analyzed in this study reflects that there is a small, yet gradually expanding community of scholars focused on OT omics. Contrary to the rest of the oncology field, which has a tendency toward large-scale multi-institutional research, OT seems to be geographically constrained to a limited number of regions and teams.

This insularity may be due to the relative rarity of the condition, lack of centralised databases, and limited funding specific to oral tumors. Nevertheless, the emergence of cross-disciplinary linkages particularly between oral pathology, bioinformatics, and molecular biology is a promising trend. Strengthening these connections will be vital to building robust data sets and standardising omics workflows across labs.

Thematic evolution over the past few decades revealed noticeable change in research focus, with early interest rooted in genetic mutations transitioning toward newer keywords such as "precision medicine," "biomarkers," and "transcriptome profiling." This thematic progression reflects the global trajectory of cancer research, suggesting that OT studies are beginning to align with broader oncologic methodologies. However, our findings also point to underexplored areas such as spatial transcriptomics, epigenomics, and AI-integrated omics that remain absent in the current OT literature. These represent high-impact research frontiers that, if pursued, could offer novel insights into tumor heterogeneity, local invasion patterns, and recurrence mechanisms.

From 2005 to 2017, the WHO listed the odontogenic keratocyst under the category of keratocystic odontogenic tumor (KCOT), and a large segment of the literature produced during this period interpreted the lesion accordingly [34]. Most studies in the scientometric data set were published during the period in which OKC was classified as a tumor (KCOT), so their study design, terminology, and analytical approach follow that tumor-based framework. After 2017, the entity was reassigned to the cyst group, yet this administrative shift did not resolve the long-standing biological ambiguity [35,36]. OKC continues to display features that extend beyond the behavior of a conventional developmental cyst. Alterations in the PTCH1–SHH signaling pathway, clonal epithelial proliferation, and a growth pattern capable of producing cortical perforation all point toward a lesion with neoplastic characteristics. Clinically, this is reflected in the management of aggressive or recurrent cases, where surgeons frequently adopt strategies aligned with tumor therapy, including peripheral ostectomy or marginal resection [37].

In this context, including OKC in our tumor data set is both historically appropriate and biologically defensible. The multi-omics patterns across regions show that molecular behavior, rather than shifting terminology, has guided how researchers interpret OKC [38]. This places OKC firmly at the crossroads of cystic architecture and tumor-like molecular activity, maintaining its relevance within the broader translational spectrum of odontogenic tumor research.

One of the important highlighting points of this bibliometric analysis is the disproportion between the number of published studies and their clinical translation. Despite several molecular studies reporting potentially actionable biomarkers, few have advanced toward validation or integration into clinical diagnostics.

This research gap in translation is an ongoing challenge in omics research and indicates the need to conduct a prospective, hypothesis-driven clinical studies with functional endpoints. To close this gap. There is a need to make an effort to include molecular data in diagnostic frameworks, build predictive models, and look into therapeutic targets that can help us make decisions about real-world treatment in oral pathology.

OTs are by their clinical presentation considered as benign but aggressive in nature which is often responsible for the local destruction of affected jaws [39-42] . However, this pattern varies based on geographical areas, with higher incidence and recurrence reported in developing countries, mostly due to late stage presentation [43]. In contrast, developed regions benefit from early detection and multidisciplinary management, though aggressive subtypes such as ameloblastic carcinoma or odontogenic sarcoma still present with poor prognostic outcomes and occasional mortality [44]. The emergence of estrogen-responsive gene profiling, newer WHO-aligned reclassifications, and atypical hybrid lesions underscores the need for systemic, histological, and longitudinal molecular integration in future odontogenic tumor research [45-47]. These indicate the need for region-specific molecular data and context-aware treatment protocols.

CONCLUSION

Recent clinical and molecular reports from regional epidemiological studies to gene expression investigations in odontogenic tissues reinforce the growing clinical interest and diagnostic complexity, further validating the need for comprehensive, multi-omics based research frameworks. This study offers the bibliometric and translational mapping of multi-omics research in odontogenic tumors, highlighting both its emerging potential and current limitations. While there has been a measurable increase in omics-based publications and thematic diversification, the field remains at a nascent stage compared to other tumor systems. While OTs may account for up to 2–3% of all oral pathologies and in some regions even more their impact is often underestimated. Despite being serious and sometimes aggressive, omics driven research into OTs remains scarce, highlighting a critical gap and a major opportunity for future discovery

Future directions

The findings from this analysis highlight several promising avenues for future research. There is a clear need to expand multi-omics integration in odontogenic tumor studies, especially through combining genomics with proteomics and metabolomics to construct more holistic molecular signatures. Prospective research should also prioritise multi-center collaborations to overcome sample size limitations and improve external validity. Future studies must therefore include validation cohorts, functional studies,

and exploration of therapeutic targets. As omics technologies become increasingly accessible, their application to odontogenic tumors may aid in diagnostic and therapeutic approaches in precision oral pathology.

Author's Contributions

PK: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Resources, Software, Validation, Writing – Original Draft Preparation, Writing – Review & Editing. MY: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing.

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List of abbreviations

AOT – Adenomatoid Odontogenic Tumour

AM – Ameloblastoma

BCL-2 – B Cell Lymphoma 2

BRAF – v-Raf Murine Sarcoma Viral Oncogene Homolog B1

CTNNB1 – Catenin Beta-1

ECM – Extracellular Matrix

HIF-1α – Hypoxia-Inducible Factor 1-Alpha

KCOT – Keratocystic Odontogenic Tumour (WHO 2005–2017 terminology)

LCM – Laser Capture Microdissection

MMP – Matrix Metalloproteinase

MS – Mass Spectrometry

NGS – Next-Generation Sequencing

OKC – Odontogenic Keratocyst (reclassified KCOT)

OSCC – Oral Squamous Cell Carcinoma

PTCH1 – Patched-1 Gene

SHH – Sonic Hedgehog Signaling Pathway

SMO – Smoothened Gene

WHO – World Health Organization

REFERENCES

1. França GM, Pinheiro JC, Almeida DRMF, Silva GG, Lima KC, Santos PPA, et al. Analysis of protein immunoexpression and its interrelationship in the pathogenesis of odontomas and ameloblastic fibro-odontomas: a systematic review. Head Neck Pathol. 2021;15(3):955-66. https://doi.org/10.1007/s12105-020-01260-x. PMid:33394370.
2. Sacramento LV, Castro IJA, Figueiredo L, Carneiro B Jr, Santos JN, Henriques AC. Calcifying odontogenic cyst with AOT-like features: a case report and literature review. Braz Dent Sci. 2023;26(4):e3823. https://doi.org/10.4322/bds.2023.e3823.
3. Li S-R, Li D-W, Man Q-W. Proteomic profile of tissue-derived extracellular vesicles from benign odontogenic lesions. J Stomatol Oral Maxillofac Surg. 2024;125(4S):101921. https://doi.org/10.1016/j.jormas.2024.101921. PMid:38795909.
4. Agarwal S, Xavier SA. Conservative management of odontogenic myxoma: a case report. Ann Maxillofac Surg. 2024;14(2):224-7. https://doi.org/10.4103/ams.ams_38_24. PMid:39957876.
5. Li S, Lee D-J, Kim H-Y, Harada H, Jung YS, Jung HS. Transcriptomic comparison analysis between ameloblastoma and AM-1 cell line. Int J Stem Cells. 2022;15(4):415-21. https://doi.org/10.15283/ijsc22132. PMid:36310025.
6. Ghazi OM. Frequency of central odontogenic tumours: a retrospective study in an Iraqi population utilizing 2022 WHO head and neck tumours classification. Braz Dent Sci. 2023;26(2):e3645. https://doi.org/10.4322/bds.2023.e3645.
7. Gomez RS, El Mouatani A, Duarte-Andrade FF, Pereira TDSF, Guimarães LM, Gayden T, et al. Comprehensive genomic analysis of cemento-ossifying fibroma. Mod Pathol. 2024;37(2):100388. https://doi.org/10.1016/j.modpat.2023.100388. PMid:37995913.
8. Diniz MG, Duarte-Andrade FF, Stussi F, Vitório JG, Fonseca FP, Domingues RR, et al. Deregulation of desmosomal proteins and extracellular matrix proteases in odontogenic keratocyst. Oral Dis. 2021;27(4):952-61. https://doi.org/10.1111/odi.13598. PMid:32772410.
9. Hu K, Zhang X, Li Y, Wang Z, Li Y. Metabolite changes in oral tumours and cysts: a narrative review. BMC Oral Health. 2025;25(1):911. https://doi.org/10.1186/s12903-025-06309-3. PMid:40468275.
10. Kalogirou E-M, Thermos G, Zogopoulos V, Foutadakis S, Michalopoulos I, Agelopoulos M, et al. The immunohistochemical profile of basal cell nevus syndrome-associated and sporadic odontogenic keratocysts: a systematic review and meta-analysis. Clin Oral Investig. 2021;25(6):3351-67. https://doi.org/10.1007/s00784-021-03877-w. PMid:33730212.
11. Dong H, Wang X, Zheng Y, Li J, Liu Z, Wang A, et al. Mapping the rapid growth of multi-omics in tumour immunotherapy: bibliometric evidence of technology convergence and paradigm shifts. Hum Vaccin Immunother. 2025;21(1):2493539. https://doi.org/10.1080/21645515.2025.2493539. PMid:40275437.
12. Chen C, Wang J, Pan D, Wang X, Xu Y, Yan J, et al. Applications of multi-omics analysis in human diseases. MedComm. 2023;4(4):e315. https://doi.org/10.1002/mco2.315. PMid:37533767.

13. Duarte-Andrade FF, Pereira TDSF, Vitório JG, Diniz MG, Amorim LSD, Nawrocki A, et al. Quantitative proteomic study reveals differential expression of matricellular proteins between fibrous dysplasia and cemento-ossifying fibroma pathogenesis. J Oral Pathol Med. 2022;51(4):405-12. https://doi.org/10.1111/jop.13282. PMid:35103997.

14. Duarte-Andrade FF, Silva AMB, Vitório JG, Canuto GAB, Costa SFS, Diniz MG, et al. The importance of BRAF-V600E mutation to ameloblastoma metabolism. J Oral Pathol Med. 2019;48(4):307-14. https://doi.org/10.1111/jop.12839. PMid:30739334.

15. Hong Y, Zhang J, Zhang H, Li X, Qu J, Zhai J, et al. Heterozygous PTCH1 mutations impact the bone metabolism in patients with nevoid basal cell carcinoma syndrome likely by regulating SPARC expression. J Bone Miner Res. 2016;31(7):1413-28. https://doi.org/10.1002/jbmr.2815. PMid:26890308.

16. Araújo LP, Rosa WLO, Carpena LP, Pinto LM, Falson LAS, Ferreira NS, et al. Intentional foraminal enlargement: a systematic review with bibliometric analysis. Braz Dent Sci. 2022;25(4):e3506. https://doi.org/10.4322/bds.2022.e3506.

17. Arumugam P, Manicka Vasagam J, Jayaseelan VP. NKAP: a new m6A RNA binding protein predicts prognosis and immunotherapy response in head and neck squamous cell carcinoma. J Stomatol Oral Maxillofac Surg. 2025;126(3S):102265. https://doi.org/10.1016/j.jormas.2025.102265. PMid:39870194.

18. Thennavan A, Sharma M, Chandrashekar C, Hunter K, Radhakrishnan R. Exploring the potential of laser capture microdissection technology in integrated oral biosciences. Oral Dis. 2017;23(6):737-48. https://doi.org/10.1111/odi.12578. PMid:27580277.

19. Cui Y, Li H, Xiao T, Zhang X, Hou Y, Li H, et al. A proteomics study to explore differential proteins associated with the pathogenesis of ameloblastoma. J Oral Pathol Med. 2023;52(6):528-38. https://doi.org/10.1111/jop.13433. PMid:37057689.

20. Ivanišević Malčić A, Breen L, Josić D, Jukić Krmek S, Džombeta T, Matijević J, et al. Proteomics profiling of keratocystic odontogenic tumours reveals AIDA as novel biomarker candidate. J Oral Pathol Med. 2015;44(5):367-77. https://doi.org/10.1111/jop.12239.

21. Aria M, Cuccurullo C. Bibliometrix: an R-tool for comprehensive science mapping analysis. J Informetrics. 2017;11(4):959-75. https://doi.org/10.1016/j.joi.2017.08.007.

22. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010;84(2):523-38. https://doi.org/10.1007/s11192-009-0146-3. PMid:20585380.

23. Kupferman ME, Myers JN. Molecular biology of oral cavity squamous cell carcinoma. Otolaryngol Clin North Am. 2006;39(2):229-47. https://doi.org/10.1016/j.otc.2005.11.003. PMid:16580909.

24. Gates JC, Clark AP, Cherkas E, Shreenivas AV, Kraus D, Danzinger N, et al. Genomic profiling and precision medicine in complex ameloblastoma. Head Neck. 2023;45(4):816-26. https://doi.org/10.1002/hed.27294. PMid:36645099.

25. García-Muñoz A, Bologna-Molina R, Aldape-Barrios B, Licéaga-Escalera C, Montoya-Pérez LA, Rodríguez MA. Identification of proteins with increased levels in ameloblastic carcinoma. J Oral Maxillofac Surg. 2014;72(6):1183-96. https://doi.org/10.1016/j.joms.2013.11.029. PMid:24485979.

26. Leite-Lima F, Bastos VC, Vitório JG, Duarte-Andrade FF, Pereira TDSF, Martins-Chaves RR, et al. Unveiling metabolic changes in marsupialized odontogenic keratocyst: a pilot study. Oral Dis. 2022;28(8):2219-29. https://doi.org/10.1111/odi.13913. PMid:33978981.

27. Ivanišević Malčić A, Breen L, Josić D, Jukić Krmek S, Džombeta T, Matijević J, et al. Proteomics profiling of keratocystic odontogenic tumours reveals AIDA as novel biomarker candidate. J Oral Pathol Med. 2015;44(5):367-77. https://doi.org/10.1111/jop.12239. PMid:25040847.

28. Mikami T, Bologna-Molina R, Mosqueda-Taylor A, Ogawa I, Pereira-Prado V, Fujiwara N, et al. Pathogenesis of primordial odontogenic tumour based on tumourigenesis and odontogenesis. Oral Dis. 2018;24(7):1226-34. https://doi.org/10.1111/odi.12914. PMid:29908099.

29. Bose P, Pleasance ED, Jones M, Shen Y, Ch'ng C, Reisle C, et al. Integrative genomic analysis of ghost cell odontogenic carcinoma. Oral Oncol. 2015;51(9):e71-5. https://doi.org/10.1016/j.oraloncology.2015.06.013. PMid:26173781.

30. Sanguansin S, Kengkarn S, Klongnoi B, Chujan S, Roytrakul S, Kitkumthorn N. Exploring protein profiles and hub genes in ameloblastoma. Biomed Rep. 2024;20(4):64. https://doi.org/10.3892/br.2024.1752. PMid:38476605.

31. Altaie AM, Venkatachalam T, Samaranayake LP, Soliman SSM, Hamoudi R. Comparative metabolomics reveals the microenvironment of common t-helper cells and differential immune cells linked to unique periapical lesions. Front Immunol. 2021;12:707267. https://doi.org/10.3389/fimmu.2021.707267. PMid:34539639.

32. Li J, Feng C, Pang X, Li X, Dou X, Jiang E, et al. L-cysteine contributes to destructive activities of odontogenic cysts/tumour. Discov Oncol. 2024;15(1):109. https://doi.org/10.1007/s12672-024-00959-5. PMid:38589585.

33. Krishnan RP, Pandiar D, Ramani P. Primordial odontogenic tumour: a case Report. Indian J Dent Res. 2024;35(4):486-8. https://doi.org/10.4103/ijdr.ijdr_402_22. PMid:39907047.

34. Maurette PE, Jorge J, Moraes M. Conservative treatment protocol of odontogenic keratocyst: a preliminary study. J Oral Maxillofac Surg. 2006;64(3):379-83. https://doi.org/10.1016/j.joms.2005.11.007. PMid:16487797.

35. Pogrel MA, Jordan RC. Marsupialization as a definitive treatment for the odontogenic keratocyst. J Oral Maxillofac Surg. 2004;62(6):651-5. https://doi.org/10.1016/j.joms.2003.08.029. PMid:15170272.

36. Yildirim G, Ataoglu H, Kalayci A, Ozkan BT, Kucuk K, Esen A. Conservative treatment protocol for keratocystic odontogenic tumour: a follow-up study of 3 cases. J Oral Maxillofac Res. 2010;1(3):e7. https://doi.org/10.5037/jomr.2010.1307. PMid:24421977.

37. Nath P, Menon S, Sham ME, Kumar V, Archana S. Conservative management of odontogenic keratocyst in a tertiary hospital. Ann Maxillofac Surg. 2020;10(1):122-6. https://doi.org/10.4103/ams.ams_260_18. PMid:32855927.

38. Anand R, Kumar Y, Bhagat N. Conservative approach for the management of odontogenic keratocyst: our experience. Cureus. 2024;16(9):e69306. https://doi.org/10.7759/cureus.69306. PMid:39398761.

39. Wang S, Yu L, Chen L, Zeng T, Xing X, Wei Z. Discovery of metabolite biomarkers for odontogenic keratocysts. Metabolomics. 2024;20(2):30. https://doi.org/10.1007/s11306-024-02101-6. PMid:38416246.

40. Valladares KJP, Balbinot KM, Lopes de Moraes AT, Kataoka MSDS, Ramos AMPC, Ramos RTJ, et al. HIF-1 is associated with resistance to hypoxia-induced apoptosis in ameloblastoma. Int J Dent. 2021;2021:3060375. https://doi.org/10.1155/2021/3060375. PMid:34987583.

41. Havighorst A, Crossland J, Kiaris H. Peromyscus as a model of human disease. Semin Cell Dev Biol. 2017;61:150-5. https://doi.org/10.1016/j.semcdb.2016.06.020. PMid:27375227.

42. Kumar VS, Kumar PR, Yadalam PK, Anegundi RV, Shrivastava D, Alfurhud AA, et al. Machine learning in the detection of dental cyst, tumour, and abscess lesions. BMC Oral Health. 2023;23(1):833. https://doi.org/10.1186/s12903-023-03571-1. PMid:37932703.

43. Kimble P, Corso AM, Beattie M, Campos MS, Cavalcanti B. Biomimetics and the restoration of the endodontically treated tooth. Braz Dent Sci. 2023;26(1):e3668. https://doi.org/10.4322/bds.2023.e3668.

44. Jaiswal A, Gautam P, Pietilä EA, Timonen S, Nordström N, Akimov Y, et al. Multi-modal meta-analysis of cancer cell line omics profiles identifies ECHDC1 as a novel breast tumour suppressor. Mol Syst Biol. 2021;17(3):e9526. https://doi.org/10.15252/msb.20209526. PMid:33750001.

45. Anjos ID, Nogueira VO, Taranto MFR, Ramazzotto LA, Nelson-Filho P, Küchler EC, et al. Estrogen deficiency influences TNF-alfa and IL-1beta gene expression in the odontogenic region of dental hypofunctional condition. Braz Dent Sci. 2023;26(2):e3790.

46. Sweeney RT, McClary AC, Myers BR, Biscocho J, Neahring L, Kwei KA, et al. Identification of recurrent SMO and BRAF mutations in ameloblastomas. Nat Genet. 2014;46(7):722-5. https://doi.org/10.1038/ng.2986. PMid:24859340.

47. Miyazaki S, Kadota A, Mitsui I, Murakami T. Amyloid signature proteins in feline amyloidosis. J Comp Pathol. 2020;177:10-7. https://doi.org/10.1016/j.jcpa.2020.03.007. PMid:32505236.

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