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Review Article

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Multi-Omics Approaches in Dentistry: Advancing Precision Diagnosis and Personalized Treatment in Oral Diseases

Evelin Ribera Rowley[1*], Pierina Flores[2], Aury Bailon[3], Raibelliz Leon[4], Alejandra Deossa[5], Johanna Quintana Theis[6]

[1]Roseman University CODM, USA

[2]Miami Dade College, United States | Universidad Central de Venezuela, Venezuela

[3]La Universidad de Zulia, Maracaibo, Venezuela

[4]Specialist in Orthodontics, Universidad Latinoamericana, Mexico City, Mexico; School of Dentistry, Universidad del Zulia, Maracaibo, Venezuela

[5]University of Colorado School of Dental Medicine, Aurora, CO, United States | DDS, Universidad CES, Colombia

[6]Universidad Santa Maria, Caracas, Venezuela

***Correspondence author:** Evelin Ribera Rowley, Roseman University CODM, USA; Email: research@idpathways.com

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Abstract

Dentistry has long relied on clinical examination and radiographic findings, which often detect disease only after tissue damage has occurred. Multi-omics technologies, including genomics, transcriptomics, proteomics, metabolomics and microbiomics, offer a transformative approach to oral health by enabling molecular-level diagnosis, individualized risk stratification and personalized treatment. This narrative review examines the current evidence on multi-omics applications in dentistry, focusing on dental caries, periodontal disease, oral cancer and xerostomia. Biological fluids such as saliva and gingival crevicular fluid serve as accessible, non-invasive sources of omics data that reflect local and systemic disease states. The integration of multi-omics platforms yields a more comprehensive picture of oral disease pathogenesis than any single diagnostic parameter can offer. Salivary biomarkers have shown particular promise for early disease detection and treatment monitoring. Despite these advances, significant barriers including high cost, lack of standardization and limited clinical validation continue to restrict routine implementation. The convergence of multi-omics with artificial intelligence represents a critical next step toward a predictive, preventive and personalized model of dental care.

Keywords: Multi-omics; Precision Dentistry; Oral Disease; Oral Diagnostics; Biomarkers; Genomic; Proteomics; Metabolomics; Microbiomics

Introduction

For a long time, dentistry has relied on clinical exams, radiographs and symptom-based decisions to diagnose and treat oral diseases [1]. While these methods have made a real difference in oral health outcomes, they have an important limitation: disease is usually identified only after tissue damage has already happened. This reactive approach often leads to delayed diagnoses, generalized treatment plans and outcomes that vary widely from one patient to another, largely because individual biology is rarely considered [2].

Conditions like dental caries, periodontitis and potentially malignant oral disorders are complex and multifactorial. They are shaped by genetic susceptibility, the oral microbiome, immune responses, lifestyle and environmental factors [2-3]. Yet the tools used most often in clinical practice, such as periodontal charting, radiographic bone assessment and visual inspection, offer only a partial view of what is happening at the molecular level. As a result, disease tends to be caught late and treatment decisions tend to be reactive rather than preventive [3].

In recent years, precision medicine has emerged as a new model in healthcare, one that moves away from a one-size-fits-all approach and instead aims to tailor care to each patient's unique biological profile [2]. Multi-omics technologies, including genomics, transcriptomics, proteomics, metabolomics and epigenomics, are at the core of this shift. Together, they allow researchers and clinicians to build comprehensive molecular profiles of individual patients and identify biomarkers linked to disease susceptibility, early pathogenesis and treatment response [4].

In dentistry, biological fluids such as saliva and gingival crevicular fluid make omics-based diagnostics especially appealing, since they are easy to collect non-invasively and reflect the local oral environment in real time [4]. Multi-omics approaches have already shown promise in this field. Genomic studies have identified genetic variants and polygenic risk scores associated with caries, periodontitis and oral cancer. Transcriptomic and proteomic analyses have uncovered dysregulated inflammatory pathways and host-microbiome interactions [5]. Metabolic profiling has revealed disease-specific signatures linked to tissue breakdown and immune dysfunction. When considered together, this data provides a much more complete picture of oral disease biology than any single diagnostic parameter could offer [6].

The oral microbiome plays a particularly important role in this context. Its composition and function are closely tied to both local and systemic health and shifts in microbial ecology have been linked to conditions ranging from caries and periodontitis to systemic disease. Understanding these interactions through omics approaches opens the door to more targeted and individualized treatment strategies [7].

Multi-omics data can support individualized risk stratification, prevention strategies and treatment plans tailored to each patient's molecular profile. These goals align well with the broader principles of personalized healthcare, including improved treatment outcomes, reduced overtreatment and lower long-term costs [6,7]. That said, significant barriers remain. Integrating data across multiple omics platforms, standardizing methods, reducing costs and validating findings in clinical settings are all challenges that still need to be addressed before these tools can be used routinely in dental practice [4].

Despite these hurdles, the growing body of evidence supports a meaningful shift in how we approach oral health: moving from a damage-based diagnostic model toward one that is more predictive, preventive and personalized [1-3]. This narrative review aims to analyze the role of multi-omics technologies in transforming dentistry into a more precise, predictive and personalized model of care, examining their current evidence base, clinical applications and the barriers that must be overcome before they can be integrated into routine practice.

Types of Omics Applied to Dentistry

Genomics

Genomics looks at a person's complete genetic makeup and how genes interact with environmental factors. In dentistry, this helps us understand why some patients are more prone to conditions like dental caries, periodontal disease, oral cancer or dental anomalies. The process starts with collecting a non-invasive sample, usually saliva or a buccal swab, followed by DNA extraction and quality assessment [7]. From there, techniques such as Polymerase Chain Reaction (PCR), Single Nucleotide Polymorphism (SNP) genotyping and Next-Generation Sequencing (NGS) are used to identify genetic variants linked to disease susceptibility. This information can then support more personalized treatment strategies for each patient [6]. Large-scale genomic studies, particularly Genome-Wide Association Studies (GWAS), have identified multiple gene loci involved in oral disease. When combined with gene expression and functional annotation data, these studies have shown that caries heritability is enriched in conserved genomic regions, which supports its classification as a complex, multifactorial condition [8].

1. Caries Susceptibility

Two main approaches are used to study the genetics of dental caries: candidate gene studies, which are hypothesis-driven and focus on specific genes or variants and genome-wide studies, which scan the entire genome and are considered hypothesis-generating. Both approaches have contributed to our understanding of disease risk and findings from one are often used to guide follow-up in the other [8]. Despite years of research, caries remain highly prevalent. Recent work highlights the potential of genetic and salivary biomarkers, including differential expression of genes such as BTF3 and TRAV4, to help with risk assessment and personalized prevention [9].

2. *Periodontal Susceptibility*

GWAS have also improved our understanding of periodontal disease genetics. Schaefer et al. identified an association between aggressive periodontitis and the rs1537415 variant in the GLT6D1 gene, while other studies have linked RS149133391 in TSNAX-DISC1 to chronic periodontitis. Although several loci have been identified, only a few have reached genome-wide significance and been replicated across studies, which reflects just how genetically complex periodontal disease really is [10].

Proteomics

Saliva is much more than just a lubricant; it plays a key role in oral physiology and carries real diagnostic potential. Advances in proteomic technologies have identified four major families of salivary secretory proteins: Proline-Rich Proteins (PRPs), statherins, cystatins and histatins. These proteins are involved in enamel protection, microbial adhesion and immune defense [11,12]. Techniques such as high-performance liquid chromatography, two-dimensional electrophoresis and mass spectrometry have enabled the identification of over 2,400 salivary proteins [11].

Proteomic studies have found meaningful differences in protein composition between caries-free and caries-susceptible individuals. Higher levels of acidic PRPs, cystatins and lipocalin tend to appear in caries-free subjects, while proteins such as amylase, immunoglobulin A and lactoferrin are associated with protective effects [13]. In periodontal disease, inflammatory markers such as IL-1β, TNF-α, PGE2 and IL-6, along with enzymes like MMP-8 and MMP-9, are elevated and reflect disease activity. Additional markers including CRP, calprotectin, IL-17A and NLRP3 further strengthen the diagnostic value of salivary proteomics [11].

Metabolomics

Metabolomics focuses on the small molecules and metabolic byproducts that reflect what is happening inside cells. In dentistry, metabolites found in saliva and gingival crevicular fluid have shown real promise for the early detection of oral diseases. Changes in organic acids and amino acids, for example, have been linked to both dental caries and periodontal inflammation [14-15]. Techniques like nuclear magnetic resonance and mass spectrometry can distinguish between healthy and diseased states with reasonable accuracy. This makes metabolomics useful not only for early diagnosis, but also for monitoring disease progression and evaluating how well a patient is responding to treatment [14].

Microbiomics

Oral microbiomics studies the microbial communities that live in the mouth and their relationship to health and disease. Under healthy conditions, these communities exist in a delicate balance. When that balance is disrupted, a state known as dysbiosis can develop and this has been closely linked to both dental caries and periodontal disease [16]. Environmental factors such as diet, changes in pH and shifts in the host immune response can promote the growth of harmful bacteria. In caries, acid-producing bacteria drive enamel demineralization, while in periodontal disease, dysbiotic biofilms trigger chronic inflammation and tissue destruction [17]. Understanding these ecological shifts from symbiosis to dysbiosis is key to harnessing the oral microbiome as a tool for early diagnosis and prevention [16-17].

Clinical Applications in Dentistry

Dental Caries

One of the most exciting things about omics sciences in dentistry is that they allow us to understand each patient's individual risk in a way that was simply not possible before. Instead of treating everyone the same, clinicians can now begin to identify who is truly at higher risk for caries based on their genetic profile, salivary composition and daily habits[18]. For example, a patient who carries genetic variants associated with weaker enamel formation or who shows elevated levels of acidogenic bacteria in their saliva, can be placed on a more intensive preventive protocol from early on, rather than waiting for a cavity to appear [19]. Salivary proteomic studies have shown that specific proteins can serve as useful indicators of caries risk. Proteins such as statherin and cystatins are known to play a protective role in enamel integrity and differences in their expression between caries-free and caries-susceptible individuals have been well documented. This opens the door to saliva-based tests that could allow earlier, more accurate diagnosis and truly personalized preventive care, all without any invasive procedures [20].

Periodontal Disease

Omics sciences have also transformed the way we understand periodontal disease. Traditionally, diagnosis has relied on probing depths, bleeding on probing and radiographic bone loss, but by the time these signs appear, damage has already occurred. Through the analysis of biomarkers in saliva and gingival crevicular fluid, including inflammatory proteins, gene expression changes and immune response markers, it is now possible to detect early signs of disease activity before clinical destruction becomes visible [18].

This also helps explain something clinicians have long observed but struggled to explain why two patients with similar plaque levels and hygiene habits can have completely different disease trajectories. The answer often lies in how each person's immune system responds to bacteria and omics approaches are making these individual differences visible and measurable [14-18]. We now understand that it is not just about which bacteria are present, but about how the host responds to them and this changes the entire clinical approach.

A recent multi-omics study by Baima, et al., showed that periodontitis not only alters the microbial composition of the mouth, but also affects microbial function and systemic inflammation, even extending to the gut. Importantly, after non-surgical periodontal therapy, these changes improved, particularly in saliva, suggesting that treating the mouth may have benefits that go well beyond the oral cavity [19,20]. These findings reinforce the idea that periodontitis should be understood as a systemic inflammatory condition, not simply a local bacterial infection and they support the future use of salivary biomarkers for both diagnosis and treatment monitoring.

It is important to acknowledge, however, that these omics-based approaches are not yet part of everyday clinical practice. Their cost is still high and results are not always consistent across studies. For now, they remain primarily research tools, but their potential to change how we manage periodontal disease is very real [19].

Oral Cancer

Oral cancer is a complex disease influenced not only by well-known risk factors like tobacco and alcohol, but also by underlying genetic and molecular changes. Thanks to genomics and other omics technologies, we are beginning to understand how cancer develops at the molecular level, why some patients carry a higher predisposition and why tumors can behave so differently from one person to the next [18].

Genetic biomarkers are among the most promising tools in this area. By detecting signals in DNA or proteins, they can help identify cancer at earlier stages, even before it becomes clinically visible. Omics studies have also made it possible to analyze specific mutations linked to oral cancer development, identify tumors that may be more aggressive and predict how a patient might respond to treatment [21,22]. This supports the development of more targeted therapies, designed around the genetic profile of each tumor rather than a one-size-fits-all approach.

Oral squamous cell carcinoma is the most common and aggressive oral malignancy and it is still most often diagnosed at late stages, which explains why survival rates have not improved significantly in recent years [18].Transcriptomic studies are helping to characterize how genes are expressed within tumors and their surrounding microenvironment, which in turn helps identify more aggressive disease, predict response to immunotherapy and uncover new therapeutic targets [19]. Another promising development is liquid biopsy, which allows cancer to be detected through a simple blood sample, offering a non-invasive way to monitor disease progression and detect recurrence [21-23].

Xerostomia and Systemic Diseases with Oral Manifestations

Xerostomia is more than just dry mouth. At the molecular level, it represents a complex alteration in salivary composition, not simply a reduction in volume. A recent proteomic study found that patients with xerostomia show significant changes in multiple salivary proteins involved in lubrication, microbial defense and regulation of the oral environment. This helps explain the clinical symptoms these patients experience, including difficulty speaking and swallowing and their increased risk of infections and caries [22].

From a broader perspective, saliva is not just a local fluid. It reflects what is happening throughout the body, including metabolic, hormonal and immunological status [18].The salivaomics approach; analyzing proteins, RNA and metabolites from saliva; makes it possible to detect alterations early, monitor disease progression and evaluate treatment response, all without invasive procedures [20]. While these technologies have not yet reached routine clinical use, they represent a meaningful step toward faster, more precise and more personalized diagnostics in dentistry.

Advantages in Dentistry

The development of multi-omics techniques has opened new possibilities in oral health research and pushed the field closer to true precision dentistry [23]. One of the most significant advantages is the ability to detect oral disease before it becomes clinically visible. By integrating data from genomics, proteomics, metabolomics and microbiome analysis, it becomes possible to identify biological changes at the molecular level long before any symptoms or tissue damage appear. This depth of information gives clinicians a much clearer picture of the processes driving disease, making it possible to intervene earlier and with greater accuracy [24].

Salivary biomarkers have become an especially exciting development in this area, offering a completely non-invasive way to pick up on early changes linked to inflammation, microbial dysbiosis and disease progression. Saliva contains proteins, metabolites and genetic material that reflect what is happening in the body and analyzing these components is already showing real promise for early oral disease identification [25,26].

Multi-omics approaches applied to the oral microbiome have also proven valuable for detecting preclinical microbial shifts. By identifying unique molecular profiles associated with diseases like periodontitis and dental caries before they fully develop, these tools make it possible to build more accurate and predictive diagnostic models [24]. Taken together, earlier detection and more targeted interventions are moving dentistry closer to a precision model that translates directly into better long-term outcomes for patients [23,24].

Another meaningful advantage is the potential for truly individualized treatment. Rather than applying the same protocol to every patient, combining genomic, proteomic, metabolomic and microbiome data allows clinicians to understand each patient's specific host response and microbial composition. In conditions like periodontitis, this information can be used to screen for susceptibility and inflammatory patterns, making targeted therapeutic decisions far more achievable [27].

Finally, multi-omics has a strong role to play in prevention. Understanding the oral microbiome and other biological markers makes it possible to profile a patient's risk before disease even begins. This enables early recognition and management of microbial imbalances before they lead to clinical pathology, helping maintain microbial equilibrium and reducing the likelihood of oral disease developing in the first place [24,28,29]. Altogether, these tools are contributing to a model of care in dentistry that is more predictive, more preventive and more personalized [29].

Limitations

Multi-omics has genuinely expanded what is possible in precision dentistry but moving it from the research setting into everyday clinical practice is still a significant challenge. The barriers are not really about science; they are about cost, consistency and the practical realities of running a dental clinic [30].

One of the most immediate obstacles is cost. Multi-omics workflows rely on technologies like next-generation sequencing, mass spectrometry and advanced computing platforms, all of which require specialized staff and ongoing investment in infrastructure [30]. For most dental schools, community clinics and private practices, this level of resource commitment is simply not realistic. Even when the technology is accessible, the costs associated with software, data storage and interdisciplinary support do not disappear. This gap becomes even wider in settings where oral health resources are already stretched thin, making it harder to bring scientific advances to the patients who may need them most [31].

Lack of standardization is another real problem. Studies in this field frequently differ in how samples are collected, stored, processed and analyzed. A finding that looks promising in one laboratory may not hold up when researchers elsewhere try to replicate it [31]. In dentistry specifically, even small differences in how saliva or gingival crevicular fluid samples are handled before analysis can affect the results. Without agreed-upon methods and thresholds, it is difficult to compare studies or build the kind of reliable evidence base needed to bring a biomarker into clinical use [32].

Clinical integration is also harder than it might seem. Introducing multi-omics into a dental appointment is not like adding one more diagnostic test. It means generating large, complex datasets that need to be interpreted in the context of a patient's full clinical picture [32]. Most clinicians are not trained to work with genomic, proteomic or microbiome data and translating that information into a practical decision at chairside requires new workflows, digital tools and collaboration with specialists. There are also real questions about how to handle sensitive biological data responsibly and equitably, which adds another layer of complexity [33].

Finally, there is the question of validation. Many of the biomarkers described in the literature are still promising candidates, not yet tested across large and diverse patient groups. Oral diseases are influenced by many factors; genetics, the microbiome, lifestyle and environment and a marker that performs well in one study population may not work the same way in another [34]. The oral microbiome in particular is highly dynamic, which makes it difficult to reduce its complexity into a single, reliable clinical test. More multicenter validation studies, greater reproducibility and platforms that clinicians can actually use are still needed before multi-omics can become a regular part of dental care [35]. In the end, closing these gaps will require more than better technology, it will take standardized protocols, validated tools and training that make these approaches workable in the real world of dentistry [36,37-41].

Conclusion

Multi-omics is transforming the way we understand and approach oral health. By working at the level of genes, proteins, metabolites and the oral microbiome, these technologies have already helped identify important biomarkers for early diagnosis, including TP53, IL-1 and MMPs. When combined with AI and advanced imaging, the potential for earlier detection, better disease prediction and more personalized treatment becomes even greater. Although multi-omics remains largely a research tool for now, its trajectory toward routine clinical practice is clear. Making that transition a reality will require better infrastructure, standardized protocols, multicenter validation and the kind of interdisciplinary collaboration between researchers, clinicians and policymakers that ensures these technologies are not only effective but also accessible and equitable for all patients.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

Not applicable.

Authors’ Contributions

All authors contributed equally to this paper.

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