8 Personalized Medicine Approaches to the Prevention, Diagnosis, and Treatment of Chronic Periodontitis

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Abstract

Over the years, the multifactorial and interactive nature of periodontal disease challenged clinicians in an attempt to delineate a pattern for its destructive progression. Periodontal disease is caused by persistent inflammation of the periodontium in response to the colonization of microbes upon the tooth surface near the gingival margin and a subsequent biofilm formation resulting in irreversible attachment loss of marginal alveolar bone and associated periodontal ligament and migration of the junctional epithelium. In spite of the infectious nature of periodontal disease, identification of the oral microbiome and a complete understanding of its pathogenic pathway seem the most logical step toward the development of newer and effective approaches for periodontal therapy.

Introduction

Periodontitis is a multifactorial inflammatory disease that disrupts the periodontium, which collectively includes the gingiva, alveolar bone, periodontal ligament, and cementum. This disease is pervasive throughout human history and remains a public health concern today, affecting individuals on a global scale [1, 2]. Defining features of this disease include the spread of inflammatory infiltrate progressively deeper into the periodontal tissue, resulting in irreversible attachment loss of marginal alveolar bone and associated periodontal ligament and migration of the junctional epithelium [3].

Clinical presentation of periodontitis involves bone loss, periodontal pocket formation, and

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possibly gingival recession; however, patterns of bone loss can be more variable between patients [4]. Periodontitis can be broadly categorized as either chronic or aggressive and further characterized by the extent of bone loss and severity of the disease [5]. Slowly progressing chronic periodontitis characteristically displays generalized horizontal bone loss, which affects most teeth and occurs over an extended period of time [6, 7]. Alternatively, in rapidly advancing aggressive periodontitis, bone loss can be highly irregular at specific sites, creating deeper pockets and infrabony defects in a short period of time [8]. In addition to local effects, recent studies have shown systemic effects of periodontal diseases through increased risk of atherosclerosis, rheumatoid arthritis, respiratory infections, adverse pregnancy outcomes, and cancer [9–15].

Risk Factors of Periodontal Disease Initiation and Progression

Periodontal disease is caused by persistent inflammation of the periodontium in response to the colonization of microbes on the tooth surface near the gingival margin and subsequent biofilm formation [16]. Bacterial colonization is an unavoidable event; salivary glycoproteins form a pellicle upon the tooth surface shortly following a professional cleaning [17]. Within minutes, primary colonizing bacteria (primarily gram-positive streptococci) adhere to the pellicle and begin proliferating [18]. Following the primary colonizers, a diverse group of microorganisms colonize, forming a unique microenvironment that increases in diversity as time passes [19].

Biofilm diversity and maturation depend on retention features and environmental factors, such as nutrients and oral hygiene practices [20, 21]. Plaque is physically retained by calculus deposits, anatomical features such as crowded dentition, and iatrogenic features such as overhanging restorations [22]. Though onset of periodontal disease is determined by presence of bacterial plaque biofilm, many studies have shown that plaque biofilm is necessary but insufficient to initiate the disease process, suggesting that there are other patient-specific factors involved [23].

To this end, susceptibility of the patient to disease onset and progression is guided by a number of different factors, as the host is ultimately responsible for periodontal tissue destruction in response to the plaque biofilm formation [24]. Host response and susceptibility are further guided by genetic, environmental, and lifestyle factors, which directly affect the progression of an existing disease process [25]. These patient-specific risk factors for progressive periodontal disease include smoking, genetic factors, epigenetic modifications, diabetes, and stress. Understanding the mechanisms by which these components function in the context of health and disease can help clinicians elucidate personalized preventative strategies for at-risk patients.

Smoking

Smoking has been well established as a risk factor for periodontal disease. It has been reported to increase the risk of periodontal disease two- to eightfold [26]. Furthermore, there is a dose-response relationship between the number of cigarettes smoked per day and the odds ratio of periodontal disease, whereby there was an increased risk of periodontal disease in patients who smoked a higher number of cigarettes [27]. Furthermore, the study by Tomar and Asma [27], with the use of epidemiologic formulas, calculated that 41.9 % of periodontitis cases in the United States' adult population were attributed to current smoking. Several clinical studies demonstrate further that smokers have both increased susceptibility and severity of disease and disease progression [28–31]. Despite exacerbated periodontal disease progression, smokers present clinically with decreased inflammation, including decreased gingival bleeding, erythema, and gingival exudate [32–34].

Smoking may affect periodontal tissue breakdown in a number of different ways, including disruption of periodontal cell migration and/or function, diminished microcirculation, and dysregulated inflammatory response [35]. Ryder

et al. demonstrated that smoke exposure to primary peripheral neutrophils impaired migration through upregulation of adhesion integrins, downregulation of L-selectin, and alterations in F-actin kinetics [36, 37]. Gingival fibroblasts and osteoblasts exposed to cigarette smoke increased production of matrix metalloproteinases (MMPs) and decreased production of tissue inhibitors of MMPs (TIMPs) [38–40]. In addition, epithelial cells and periodontal ligament cells showed decreased survival and proliferation in the presence of cigarette smoke [41, 42]. Furthermore, animal studies confirmed these in vitro data demonstrating smoking and tobacco-associated particulate increased alveolar bone loss, increased MMP levels, decreased fibroblast-like cell proliferation, and reduced periodontal tissue repair [43–46].

In humans, however, the mechanism of periodontal breakdown observed in response to tobacco use has not been fully elucidated. Consensus of literature is present on the deleterious effects of typical periodontal treatment therapy, scaling, and root planning in smokers [47–49]. The use of adjuncts such as antimicrobials and anti-inflammatory agents has been utilized in the treatment of smokers. However, inconsistencies in clinical reports have yielded meta-analyses with inconclusive results [50]. Taken together, these results highlight the complex nature of the host response within the tobacco-periodontal disease relationship and variant response among sampled patients.

Diabetes

Diabetes is characterized by chronic hyperglycemia as a result of defects in insulin secretion, insulin action, or both. In addition, diabetic patients have disturbances in carbohydrate, protein, and fat metabolism [51]. These combined metabolic disturbances can result in long-term damage to many vital organs and increase risk of other diseases, including periodontal disease [52–54].

Diabetes affects periodontal disease by increasing its prevalence, severity, extent, and progression [55]. The relationship between diabetes and periodontal disease was suspected with the observation that the severity of periodontitis was statistically worse in individuals with diabetes compared to those individuals without diabetes [56, 57]. Longitudinal studies have demonstrated that poor glycemic control is associated with increased rate of attachment loss and alveolar bone loss for both males and females [58–60].

The relationship between diabetes and periodontal disease has been expressed as bidirectional (1) due to the associations reported of periodontal disease severity and glycemic control and (2) through the biological mechanism that inflammation can dysregulate glycemia [61]. To this point, patients with worsened glycemic control showed increased risk of periodontal disease [62]. Likewise, periodontal disease adversely affected glycemic control in diabetic patients [63, 64]. This relationship is corroborated evidence that treatment of periodontitis can decrease elevated levels of glycated hemoglobin [65–67].

Treatment of periodontal disease associated with diabetes is not without complications. Diabetic patients generally have delayed wound healing and a diminished response to periodontal treatment [68]. Mechanisms for these outcomes include a hyperreactive inflammatory response, increased cellular apoptosis, increased levels of pro-inflammatory mediators such as advanced glycation end-products (AGEs), and altered immune response such as impaired phagocytosis and neutrophil chemotaxis [69–71].

Due to rising global incidence of diabetes mellitus, clinicians must be able to identify this disease in both diagnosed and undiagnosed patients. Additionally, dental clinicians must work with both the individual patient and comprehensive medical team to manage both local and systemic effects of diabetes mellitus.

Genetic Factors

Periodontal disease is initiated by colonization of microorganisms and subsequent biofilm formation; however, genetic factors may also modify

the susceptibility of the host. Genetic factors that may influence the onset of periodontal disease include specific genes, gene-gene interactions, and gene-environmental interactions [55].

Strong evidence that genetic factors influence the risk of periodontitis is rooted in studies between adult twins [72]. Specifically, Michalowicz et al. demonstrated that monozygotic twins were more similar than dizygotic twins [73]. Additionally, this work showed that chronic periodontitis was estimated to have an approximately 50 % heritability, thus signifying that about half of the variance in periodontal disease is attributed to genetic factors. The authors further pointed out that there was no evidence for the heritability for gingivitis.

In addition to twin studies, familial aggregation studies have demonstrated that aggressive periodontitis is an inherited autosomal dominant trait in black families [74]. Other familial aggregate studies have demonstrated that aggressive periodontitis is very high among specific families, affecting siblings up to 40–50 % [75]. In the case of aggressive periodontitis, studies often concomitantly report an underlying cause of leukocyte dysfunction, which may also be genetic.

Familial aggregation studies have also reported a basis for shared environmental factors in addition to shared genetic factors, which in many cases cannot be distinguished. Shearer et al. demonstrated that parents with poor oral hygiene tend to have children with poor oral hygiene; however, they were unable to distinguish between genetic and environmental factors [76].

Association studies have also been conducted to determine to the relationship of genetic polymorphisms and chronic periodontitis [77, 78]. Karimbux et al. [79] identified two interleukin (IL) gene variations that increased the risk of chronic periodontitis in adult whites: IL-1A (odds ratio = 1.48) and IL-1B (odds ratio =1.54). In addition, other genetic polymorphisms have been identified to potentially influence the onset of periodontal disease, including IL-6 and Toll-like receptors (TLRs) [80–82].

Furthermore, genome-wide association studies have also been conducted and provide a larger analysis of the entire genome for more than a million polymorphisms [83]. While polymorphisms have not been statistically significantly associated with chronic periodontitis, one study reported an associated genetic polymorphism with aggressive periodontitis [84, 85]. Schaefer et al. demonstrated a single nucleotide polymorphism associated with intron 2 of glucosyltransferase 6 domain containing 1 (GLT6D1) correlated with generalized aggressive periodontitis [85]. This finding was recently replicated in the study of aggressive periodontitis in a Sudanese population [86].

The potential of genome-wide association studies provides a means to more clearly identify the mechanisms involved in the onset and progression of periodontal disease. Precisely identifying the etiology of a patient's disease will support personalized treatment and improve patient care.

Epigenetics

Changes in the gene expression that are not related to alterations in the DNA sequence serve as the basis for epigenetics. Such modifications are associated with chemical alterations of the DNA and packing proteins responsible for the shape and structure of the chromatin, leading to activation or inactivation of genes [87]. DNA methylation and histone modifications represent two of the major epigenetic modifications as result of the exposure to environmental factors. While different possible mechanisms of DNA methylation in periodontal disease have been suggested [88, 89], studies emphasizing histone modification mechanisms remain scarce and limited [90].

Epigenetic modifications have been identified among carcinogenesis and autoimmune and chronic inflammatory diseases, such as periodontitis. As discussed earlier, the multifactorial nature of periodontal disease and its destructive progression can be impacted by several risk factors [91]. In such instances, it has been hypothesized that the constant exposure of these environmental factors to the gingival tissues is capable of modifying gene expression and thus increasing the susceptibility for disease activity

or explains the presence of unresponsive sites despite receiving periodontal therapy.

The epigenetic patterns of environmental factors associated with periodontal disease have not been fully elucidated. Identification of these DNA modifications may represent a viable approach for patient stratification, adjustments in recalls for dental care, and more personalized treatment according to the patient's disease susceptibility.

Stress

Stress was first identified to negatively impact the periodontal tissues in necrotizing periodontal diseases [92]. However, there might be connections between stress and chronic diseases, including periodontitis [93, 94]. Several studies have reported that stress increased the odds of periodontal disease more than twofold [95, 96]. Furthermore, Genco et al. [95] reported that individuals who were under stress, such as financial strain, but who had developed effective coping methods had no increased risk of periodontal disease relative to individuals without stress.

The mechanisms by which stress affects a patient's susceptibility to periodontal diseases include both immune modulation and behavior modification. Stress modulates immune response via neurons located in the hypothalamic-pituitary-adrenal axis that produce biological mediators that modulate immune cell activity [97]. When activated through stress, the hypothalamic-pituitary-adrenal axis stimulates secretion of corticotropin-releasing hormone and glucocorticoid hormones [98]. Immune cells have receptors for these biological mediators, and stimulation of these receptors may lead to immune dysregulation [97]. Immune dysfunction as a result of stress is expressed in a number of ways, including decreased natural killer cells, decreased antibody production to vaccination, increased susceptibility to infectious diseases, and latent virus activation [99]. Immune suppression caused through the hypothalamic-pituitary-adrenal axis increases susceptibility to periodontal infections [100].

Additionally, the autonomic nervous system may be activated by stress. Stimulation of the autonomic nervous system induces catecholamine release [101]. In turn, catecholamines promote release of proteases and prostaglandins [102]. Increased proteases and prostaglandins in the periodontal tissues can amplify periodontal tissue destruction [101, 103]. As such, there are multiple biological mechanisms by which stress influences the onset and progression of periodontal disease.

In addition to the biological mechanisms involved in stress-mediated susceptibility to periodontal disease, stress also modifies behaviors that can promote periodontal disease [103]. These behaviors include increased smoking, decreased oral hygiene, and/or fewer dental visits [95]. Combining the biological mechanisms and behavior modifications induced by stress, the effects of stress can be harmful to both the periodontal health and systemic health of patients. Identifying patients at risk for periodontal disease who have poor stress-coping skills may be important in the development of a personalized treatment strategy for those patients.

Pathogenesis of Periodontal Disease

Over the years, the multifactorial and interactive nature of periodontal disease challenged clinicians in an attempt to delineate a pattern for its destructive progression. A series of cross-sectional studies by Löe and colleagues initiated a new era in understanding periodontitis by using an untreated population of Sri Lankan tea workers to evaluate the natural progression of periodontal disease [104–107]. Their findings reported different rates of progression patterns, with a small part of the population in whom gingivitis never progressed to periodontal disease [108]. Later studies revealed a dynamic condition with random and asynchronous periods of disease exacerbation and remission, as well as periods of inactivity, suggesting linear and nonlinear destructive patterns [109, 110].

Despite its natural progression, the main finding focused on the impact of biofilm upon the gingival tissues as a true etiology for the

development of periodontal disease. The following section will discuss the ecological community of the periodontium and the host immunological and adaptive responses against the periodontopathic microorganisms.

Microbiome

In spite of the infectious nature of periodontal disease, identification of the healthy and pathogenic microorganism seems the most logical step toward the development of an effective periodontal therapy. Limited by technological advances, early studies used DNA probes; polymerase chain reactions (PCRs) and immunoessays were molecular diagnostic tests meant to fulfill this purpose. Cross-sectional studies in combination with culture techniques allowed a clear identification of early and late colonizers within the biofilm [111]. Interestingly, the short-term transition from a nonmotile gram-positive bacteria (i.e., cocci and *Actinomyces* sp.) to a motile, anaerobic gram-negative bacteria (*Veillonella* and *Bacteroides* sp.) was commonly observed as the natural recolonization pattern after providing periodontal treatment [112].

Socransky and colleagues divided the microbial populations in complexes according to their association with disease activity [110]. Members of the red complex (i.e., *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*) and orange complex (*Fusobacterium, Prevotella*, and *Campylobacter* spp.) are considered meaningful in the periodontal diagnosis due to their high correlation with deep probing depths and bleeding on probing in patients affected with chronic periodontitis. On the contrary, *Aggregatibacter actinomycetemcomitans* was associated as the main etiological microorganism of aggressive periodontitis. These findings suggested a more appropriate and effective approach by targeting specific bacteria with the use of systemic or locally delivered antibiotics [112, 113].

Recently, newer molecular approaches made possible the ability to identify unrecognized species in the etiology of periodontal diseases and thus expanded our knowledge of the diversity of these oral microbiomes [114, 115]. As a matter of fact, microorganisms of the Archaea and Eukarya domains, in addition to new bacterial candidates (i.e., *Filifactor alocis*), revealed moderate association in periodontitis-affected patients [116].

To a certain point, the understanding of the composition of the subgingival biofilm extends beyond the limits of the oral cavity. A collection of 16S ribosomal RNA gene sequencing has been used by the Human Microbiome Project to establish the dynamic association of microbial communities across different sites across the human body. Patients' interactions between their surrounding environments can shape the structure of the human microbiome. Aside from its complexity, the oral microbiome reflects unstable patterns from an intra- and interpersonal perspective when compared to other ecosystems [117].

Host Response

In a pristine periodontium, the epithelium turnover and the attachment apparatus serve as an effective barrier against the microbiological invasion and associated endotoxins in their attempt to penetrate into the underlying tissues. Saliva and gingival crevicular fluid (GCF) secretion act as defense mechanisms by removing or preventing further microbial aggregation upon the tooth surface. Furthermore, the homeostasis of the oral cavity is enhanced by humoral immune response through complement proteins and specific antibodies contained among these oral fluids.

Diffusion of bacterial endotoxins through the junctional epithelium will trigger an increased production of inflammatory mediators, including a variety of interleukins, prostaglandin E2 (PG2), histamine, and MMPs from keratinocytes, fibroblasts, macrophages, and endothelial or mast cells. Activation of these mediators leads to a hyperemic effect of the surrounding blood vessels by altering the vascular permeability. Opening of the endothelial cell junctions facilitates the extravasation of the vessel content in the extracellular matrix and the migration of leukocytes to the sulcus area in response to the chemotactic stimuli elicited by IL-8 and intercellular attachment molecule-1.

Underneath the subgingival biofilm, a cell barricade is formed following the expression of cell adhesion molecules and pro-inflammatory agents for leukocyte recruitment to prevent its further apical advancement. In early stages of inflammation, neutrophils represent the most abundant cell population within this inflammatory infiltrate, which might also include monocytes, lymphocytes, Langerhans cells, and other antigen-presenting cells. Nevertheless, the predominance of specific leukocytes will eventually shift over time from a polymorphonuclear toward a mononuclear concentrate.

Macrophages are crucial players in the transition of early to advanced lesion. Several cytokines from lipopolysaccharide-activated macrophages, such as tumor necrosis factor-α (TNF-α), IL-1B, PG2, and MMPs (such as MMP-1, MMP-3, MMP-8, MMP-9, and MMP-13), function as chemoattractant signals for mononuclear recruitment and are capable of inducing collagen degradation [118]. Macrophage-mediated expression of TIMPs has the ability to suppress collagenase activity and primarily acts as adaptive mediators. For such reason, the sole presence of macrophages, monocytes, T and B lymphocytes, and plasma cells provides evidence for the chronic nature of periodontal disease and potential risk for further disease progression [119, 120].

Receptor activator of nuclear factor kappa-B ligand (RANKL) is a cell-surface protein critical, which binds to its specific receptor RANK on hematopoietic cells for osteoclastic differentiation and activation [121]. Conversely, osteoprotegerin (OPG) binds to RANKL to inhibit the differentiation process [122, 123]. Bone resorption is regulated by the RANK/RANKL/OPG interaction. Once the balance of these bone mediators is disrupted as a result of the plaque-induced collagen degradation, an advanced lesion is established. GCF increased levels of RANKL and reduced levels of OPG have been reported during periodontal disease.

As previously discussed, the progression of the disease might differ between individuals in response to several risk factors. Eventually, tooth loss will occur if the disease remains untreated.

Management Strategies

Proper management of all systemic and local factors affecting the periodontal condition is essential to achieve or maintain a state of health, comfort, and function [124]. Adequate home care, patient education, and motivation for compliance of dental care play significant key roles in preventing plaque accumulation and future disease progression before and after providing initial periodontal therapy.

Removal of bacterial biofilm through mechanical debridement represents the foundation of periodontal therapy. Nonsurgical therapy consists of a closed-flap approach using site-specific and ultrasonic instrumentation under local and regional anesthesia. Scaling and root planning are the most widely used methods to create a viable environment to promote the formation of new attachment upon the denuded root surface. If managed properly, significant pocket reduction and limited clinical attachment gain are among the expected treatment outcomes.

Despite efforts to obtain a complete calculus removal, surgical approaches have been proposed to overcome limitations of nonsurgical therapy [125, 126]. Periodontal surgery aims to improve the access to the affected sites and create pockets accessible for regular home care. Elimination of pockets and reduction of inflammation represent the ultimate treatment goals of periodontal surgery.

A careful assessment of the defect morphology is crucial when selecting between resective and regenerative procedures. Osseous surgery involves removal of the bony supporting tissues to correct deformities resulting from periodontal disease and increase better tissue adaptation. However, aesthetic concerns may arise from these procedures due to increased gingival recession being most critical in the anterior zone. On the other hand, modern dentistry promotes the use of bone grafting, soft tissue grafts, biological agents, and barrier membranes to restore lost periodontal structures without compromising aesthetics.

Ultimately, the use of locally delivered antibiotics is advocated to be as effective as mechanical debridement for unresponsive sites; however,

these agents are limited to controlling disease activity, rather than calculus chemical dissolution [127–130]. Regardless of the approach, pocket elimination, defect correction, and reduction of inflammation reflect the successful treatment outcomes of periodontal therapy [131–133].

Periodontal maintenance is considered an extension of active periodontal therapy and consists of procedures to maintain periodontal stability. Longitudinal studies have shown the importance of periodontal maintenance following active periodontal therapy. Recurrence of periodontal disease can be observed in surgically and nonsurgically treated patients without regular or erratic maintenance recalls [134, 135]. On the contrary, long-term results of periodontal therapy can be sustained with periodic intervals [136–138].

In order to minimize risk for recurrence of periodontal disease or arrest disease progression in a timely manner, recall programs ranging between 3 and 6 months have been considered acceptable [139, 140]. Nowadays, oral hygiene and rate of microbial pocket recolonization remain as the key components to determine regular maintenance intervals; however, a personalized risk assessment of contributing factors might represent a more valid approach to establish adjustments in dental care visits [141].

Conclusions

Current clinical periodontal diagnostic criteria used in the practice setting have limited utility to predict future disease progression [142]. The potential role of host-response biomarkers and microbial profile obtained from oral fluids has been investigated as complementary diagnostic tools for periodontal disease (see Fig. 5.3). Concentrations of host-response molecules and total percentage of bacterial DNA may represent a more accurate, real-time disease activity than conventional clinical measurements [143, 144].

Identifying a single predictive biomarker for periodontal diseases would be of great significance [142, 145]. Oral health professionals are in need of diagnostic and prognostic tools to obtain fast and valuable information in order to enhance the decision-making for periodontal therapy [146, 147]. Nevertheless, present diagnostic tests require training, major resources, and increased cost-effective healthcare delivery [148]. For that reason, biomarkers and microbial assessment with portable and simpler microfluidic screening devices might lead to acceptance from the dental community and a more efficient therapy (Fig. 8.1) [149, 150].

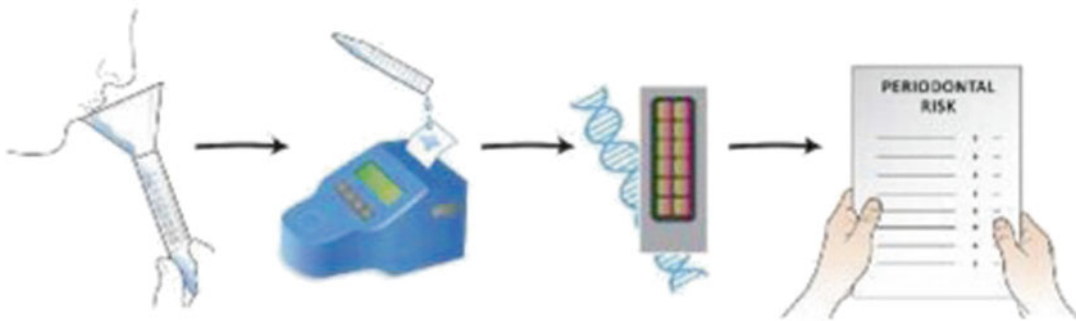

Fig. 8.1 Application of salivary diagnostics to the periodontal practice of the future. A point-of-care diagnostic may be available in which a patient provides an oral sample that is delivered to the chairside or to a laboratory device. The result is interpreted by the oral healthcare provider, who then educates the patient about the findings from the biomarker report. The diagnostic test may reveal a patient's susceptibility to disease (e.g., a genetic test) or provide a real-time assessment of the patient's disease status via the use of microbiological or protein markers of periodontal infection, destruction, or both (Reprinted from Giannobile [148]. Copyright © 2012 with permission from Elsevier)

Despite significant advances in oral fluid diagnostics, the role of DNA testing has shown promising results and represents the key component of personalized approaches. Gene polymorphisms were initially proposed as potential indicators for disease susceptibility. Kornman and collaborators demonstrated an association of IL-1B and periodontal disease in a specific population [78]. Nowadays, the assessment of cell molecular signaling from gingival tissues has been used in an attempt to develop newer alternatives of periodontal classification systems based on genome transcriptomic profiles of chronic and aggressive periodontitis [151]. Drug-assisted therapies targeting epigenetic modifications could be considered to control disease activity as observed in cancer research [152]. Pharmacoepigenetic biomarkers may potentially be used to assess the drug effectiveness and predict their response. Epigenetic inhibitors (i.e., histone deacetylase inhibitors, DNA methyltransferase inhibitors) could represent a novel approach to repair any cellular damage caused by periodontal disease or oral inflammation [87].

There should be considerable benefits to all key stakeholders as new technologies are deployed to improve the diagnosis, prognosis, and treatment of patients. The complexity of biological systems means that not all genetic lesions may manifest as important phenotypic changes and disease patterns, making the identification of potential biomarkers and new targeted treatments more difficult. This may explain in part why the promise of personalized oral healthcare has been slow to translate scientific findings directly into improvements for patient care and why only a limited number of targeted treatments are currently available. Nowadays, for some of the more common dental diseases such as periodontitis, there is insufficient evidence to support the routine use of biomarkers in either diagnosis or targeted therapies. As such, increased support for research in areas of personalized medicine could potentially have a tremendous impact in the future of patient care, especially within the context of dentistry.

Personalized oral healthcare offers the potential to revolutionize the practice of dentistry. It also provides a unique window into the relationship between new medical technologies and new models for healthcare delivery. Using personalized medicine as a test of disruptive innovation in healthcare, it will be necessary to take a different approach to technology development. Achieving this, however, is fraught with difficulty, as innovations are deemed truly disruptive only in hindsight. A robust framework for continuing assessment, close scrutiny, and oversight of developing technologies might help protect the integrity of this process while enabling the rapid deployment of scientific discovery into the patient care environment. While there is unquestioned risk in this largely untested approach to healthcare, the benefits of investing in disruptive innovations that will truly revolutionize our approach to disease diagnosis and treatment are worth the risk.

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