



ORAL  RISK

Oral Health Indication Summary

WHITE PAPER

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Abstract

Genetic screening for finite set of dental conditions that have an association with detectable genetic germline alterations that are clinically studied. Genetic influencers can include, but not limited to, direct and indirect influencers (cancer), lifestyle influencers (BMI, type II diabetes), demographic influencers (age, sex), and regional influencers (country, province). Genetic analytes include genetic risk factors variable population frequency and with well-established and published evidence for increased or decreased risk association for various dental indications included in this assay.

The oral health product captures six criteria, each with defined influencers.

Indications for Oral Health Product offering:

1. Periodontal disease
2. Tooth decay
3. Oral cancer
4. Misaligned teeth (malocclusion)
5. Cleft lip and cleft palate
6. Yellow Teeth (amelogenesis imperfecta)

Please note

Genetic variants are subject to change and evaluation up until panel is ready to be locked for development.

Overview

Many oral health conditions have a genetic basis. Despite good oral hygiene habits some individuals may have inherited an increased risk of certain dental problems. Genetic factors are implicated in periodontal disease, caries resistance, some oral cancers and other oral buccal conditions. The 2016 Global Burden of Diseases, Injuries and Risk Factors Study estimated that periodontitis and dental caries (tooth decay) were the leading 11th most prevalent disease worldwide (Shungin et al., 2019) Global economic impact of dental diseases amounted to US\$442 billion in 2010. Overall improvements in oral health may imply substantial economic benefits, not only in reduced treatment costs but also a decrease in productivity losses in the labour market.

Periodontal Disease

Brief overview: Periodontal disease is a chronic inflammatory disease that leads to the degradation of tooth-supporting structures (Shungin et al., 2019). At first a patient might present with gingivitis, which is characterized by swollen and red gums that tend to bleed. Gingivitis can progress to periodontitis, which can result in bone or tooth loss as the gum detaches from the tooth (Centre for Disease Control and Prevention, 2013). Periodontal disease is the main cause of tooth loss and is the most common oral condition in the human population (Raitapuro-Murray et al., 2014).

Scope of reported factors:

Factor	Grade A evidence	Grade B evidence	Grade C evidence	Grade D evidence	Total Number of Factors Reported
Variant (for genotyping)	3	15	11		29
Gene (for targeted sequencing)	-	-	-	-	-
Lifestyle		1			1
Demographic					In Progress
Regional					In progress

Misaligned Teeth (Malocclusion)

Brief overview: Malocclusion is the development of a complex trait condition and relationship between both dental arches, in which occlusion has deviated from what is defined ideal or normal occlusion. Human malocclusion is a disarrangement of teeth and jaws that may lead to distorted facial appearance, limited masticatory function, increased dental trauma, difficulty in speech, social interaction and thus compromise quality of life (Claudino D. and Traebert J., 2013)

Scope of reported factors:

Factor	Grade A evidence	Grade B evidence	Grade C evidence	Grade D evidence	Total Number of Factors Reported
Variants (for genotyping)	-	3	43		46
Genes (for targeted sequencing)	-	-	-	-	-
Lifestyle					In progress
Demographic					In progress
Regional					In progress

Yellow Teeth (Amelogenesis Imperfecta)

Brief overview: One of the causes of yellow teeth is amelogenesis imperfecta (AI). This hereditary condition is characterized by defects in tooth enamel and can be accompanied by tooth discoloration, pits and/or grooves and significant decay. People with AI can experience pain associated with extreme tooth sensitivity and may have difficulty eating. This is a heterogenous condition with well characterized genetic underpinnings (Crawford et al., 2007).

Scope of reported factors:

Factor	Grade A evidence	Grade B evidence	Grade C evidence	Grade D evidence	Total Number of Factors Reported
Variants (for genotyping)	-	-	-	-	-
Gene (for targeted sequencing)	16	1			17
Lifestyle					In progress
Demographic					In progress
Regional					In progress

Tooth decay

Brief overview: Tooth decay, or dental caries result from destruction of the tooth's enamel. Tooth decay can be caused by the acid produced by the bacteria responsible for breaking down food in the mouth. The acid-induced enamel erosion creates a hole (cavity) in the tooth. If left untreated, infection or more severe outcomes such as tooth loss can occur (National Institute of Dental and Craniofacial Research, 2019).

Scope of reported factors:

Factor	Grade A evidence	Grade B evidence	Grade C evidence	Grade D evidence	Total Number of Factors Reported
Variants (for genotyping)		43			43
Genes (for targeted sequencing)	-	-	-	-	-
Lifestyle					In progress
Demographic					In progress
Regional					In progress

Oral cancer

Brief overview: oral cancer is caused by an abnormal growth of cells (typically squamous cells) in the mouth, tongue, throat, or lips. Oral cancer is multifactorial, meaning, a combination of environmental and genetic factors contribute to an individual's risk of developing cancer. Treatment varies based on the stage of cancer and location, and the patient's age. Although patients over 60 years of age have the highest risk of oral cancer, the incidence has increased in the 40 years of age and under population. Early diagnosis through screening and early detection is critical as prognosis is much better with early detection (The Canadian Cancer Society, 2021)

Scope of reported factors:

Factor	Grade A evidence	Grade B evidence	Grade C evidence	Grade D evidence	Total Number of Factors Reported
Variants (for genotyping)	16	22	3		41
Genes (for sequencing)	-	-	-	-	-
Lifestyle					3
Demographic					In progress
Regional					In progress

Cleft lip and cleft palate

Brief overview: Cleft lip and palate typically involve tissue disruption above the lip, with extension into the nares and/or palate (hard or soft). These defects occur in the early stages of embryogenesis and can be unilateral or bilateral in nature. Individuals with cleft lip and/or palate can experience issues with feeding, speaking, hearing and may experience difficulties in social settings. Each of these issues can be addressed to a certain extent with surgery, dentist involvement, and therapy. Research on the genetic underpinnings of NS-CL/P can help identify the corresponding biological mechanisms and ultimately help with treatment and prognosis.

Scope of reported factors:

Factor	Grade A factors	Grade B factors	Grade C factors	Grade D factors	Total Number of Factors Reported
Variants (for genotyping)	5	26	16		47
Genes (for sequencing)	4	2			6
Lifestyle		2	4		6
Demographic					In progress
Regional					In progress

Current Testing Methodology

Currently, diagnosis for periodontal disease is achieved using a decision-making algorithm proposed by the 2017 World Workshop Classification system for periodontal and peri-implant diseases and conditions. Numerous criteria including extraoral and intraoral examination, evaluation of periodontitis stage and grade, and assessment of risk factors are combined to reach a diagnosis and differentiate between precursor diseases like gingivitis (Dietrich et al, 2019).

Dental caries detection and diagnosis are completed at routine dental examinations by general dental practitioners. The traditional method of detecting dental caries in clinical practice is a visual tactile-examination often with supporting radiographic imaging (Macey et al., 2018).

During routine visits, the dental practitioner completes an oral examination of jaw and teeth alignment for presence of malocclusion. If the jaw or teeth are out of line, the dentist may suggest a visit to the orthodontist where they will further complete a history and oral physical examination. Radiographic imaging and impression of teeth may be required to help malocclusion classification (Ravaghi V., Kavand G., Farrahi N., 2015).

Diagnosis of oral cancers begin with visits to the dentist or family doctor where they will ask about any related symptoms and perform a dental or oral exam. From this, a referral to a head and neck surgeon or ear, nose and throat (ENT) doctor to carry out other exams and tests such as: exfoliative cytology, biopsy, endoscopy, nutritional assessment, speech, swallowing and dental assessments, radiographic imaging and more. Many of these tests are used to rule out, diagnose and/or stage the cancer to see how far it has progressed (Canadian Cancer Society, 2021).

Diagnosis of Amelogenesis Imperfecta is typically achieved with a combination of x-ray imaging, assessment of the clinical phenotype, and family history. Preventative measures are of utmost importance for this condition to avoid tooth decay and other severe outcomes. In childhood, some individuals opt to protect their teeth with crown coverings. Good oral hygiene is critical for patients with AI (Crawford et al., 2007).

Our Test:

Currently, a clinically adopted genetic test that assesses predisposition to caries or periodontal disease does not exist. Conferences hosted by the American Dental Association have focused on the application of genomics to patient care, with considerations for its adoption and clinical use (Philstrom & Barnett, 2016). By working with key stakeholders in the field of dentistry, Ai Genetics can develop a predictive tool that aligns with the needs of dentists. The Ai Genetics dental product offering will bin genetic variants into risk categories, providing a meaningful assessment of the genetic profile for each patient as it relates to each of the dental indications.

The genetic variants underlying complex common diseases such as periodontal disease and dental caries can be detected using cost-effective genotyping technology such as MALDI-TOF.

Variants in genes underlying Mendelian disorders, such as Amelogenesis Imperfecta, are suitable for detection using targeted next-generation sequencing panels.