

## Nutrigenomics in periodontics- An overview

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### Abstract

Nutrigenomics is an emerging field of science and technology revealing inter-relationships between nutrients and human genome using modern tools such as transcriptomics, metabolomics, epigenomics and proteomics. It implies that nutrition and genetics both play a significant role in the maintenance of human health as well as the development of lethal diseases. Nutrition may be important in redressing the balance between microbial challenge and the host response because it has been implicated in a number of inflammatory diseases and conditions, including type II diabetes mellitus, cardiovascular diseases, rheumatoid arthritis and inflammatory bowel disease, all of which have also been associated with periodontal diseases. Based on the pathology of periodontal disease, the assumption is that specific nutrients which can modulate immune and inflammatory responses could in turn modulate periodontal health. Antioxidant vitamins and trace elements which are known to be depleted during periods of inflammation can counteract reactive oxygen species damage to cellular tissues and modulate immune-cell function through the regulation of redox-regulated transcription factors and ultimately affect the production of cytokines and prostaglandins, thus leading to periodontal changes. Thus we now have the opportunity to study nutrient-gene interactions and how diet affects the inflammatory mechanisms underlying severe periodontitis.

### Introduction

Periodontitis is defined as "an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, initiating progressive destruction of the periodontal ligament and alveolar bone with pocket development, recession, or both."<sup>(1)</sup>

Susceptibility to periodontal diseases involves the interplay between genetic, bacterial, environmental and nutritional factors. Tooth loss has been associated with nutrient deficiency and changes in food predilection. Common dietary chemicals act on the human genome, either directly or indirectly, to alter gene expression or structure. Genes are important in determining the function, but nutrition is able to modify the degree of gene expression.

During our lifetime, nutrients can modify physiologic and pathologic processes through epigenetic mechanisms that are critical for gene expression.<sup>(2)</sup>

Investigating the relation amongst nutrients and periodontal disease has been important to understand the potential role of dietary modification in the prevention and treatment of periodontal disease and the ultimate prevention of tooth loss through periodontal disease.

Improved understanding of the mechanism behind periodontal tissue destruction, the potential defensive role of nutrients and the advent of modern genomic measurement tools have led to an increased interest in the association between nutrition and periodontal disease.<sup>(3)</sup>

### What is Nutrigenomics?

Nutrigenomics is an emerging field of science and technology unrevealing inter-relationships between nutrients and human genome using modern tools such as transcriptomics, metabolomics, epigenomics and proteomics (Fig. 1). Nutrigenomics aims to reveal the relationship between nutrition and the genome and to provide the scientific basis for improved public health through dietary means. It is extremely likely that interactions between genotype and diet are important in determining the risk of the most common complex diseases, including periodontal disease.<sup>(3)</sup>

It is well established that specific nutrients can modulate immune and inflammatory responses. Based on the pathology of periodontal disease the assumption is that these nutrients could modulate periodontal health. Oral health scientists now have the opportunity to study nutrient-gene interactions and how diet affects the inflammatory mechanisms underlying severe periodontitis.<sup>(4)</sup>

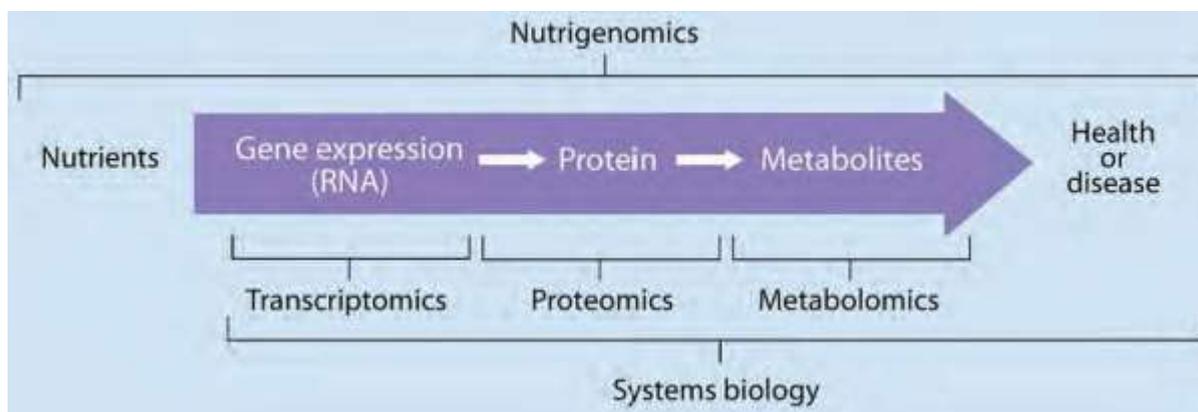


Fig. 1

### Mechanisms Revealing Nutritional Modulation OF Periodontal Inflammation

Periodontitis is initiated by the plaque biofilm, but most tissue destruction results from an abnormal inflammatory immune response in patients predisposed to the condition.<sup>(5)</sup> The response is characterized by hyperinflammation, which fails to eradicate the causative pathogens and generates prolonged release of neutrophil proteolytic enzymes, proinflammatory mediators and reactive oxygen species (ROS), which in turn destroy the periodontal attachment.<sup>(6)</sup>

Researchers have found irrefutable evidence that macronutrients and micronutrients modulate proinflammatory and anti-inflammatory cascades, which influence a person's baseline inflammatory status. The functionality of nutrients in human biology extends beyond that of being fuels for energy production and cofactors in metabolism, to acting as molecular signals that are capable of modulating gene and protein expression at a molecular level. These review highpoints mechanisms whereby key macronutrients and micronutrients modulate inflammation.<sup>(7)</sup>

Diet-induced hyperlipidemia induces oxidative stress and downstream inflammation, and lipoproteins formed by liver hepatocytes can be converted to free fatty acids within the circulation and taken up by adipocytes, thus acting as a basis of proinflammatory adipokines. Furthermore, in states of oxidative stress, lipid peroxidation (a chain reaction induced by ROS attack on the polyunsaturated fatty acid [PUFA] side-chains of lipid membranes) arises, lowdensity lipoproteins are oxidized (oxLDL) and the oxLDLs bind to a group of pattern recognition receptors called "toll-like receptors" (TLR-2/4) on inflammatory cell membranes, triggering NF- $\kappa$   $\beta$  activation via the protein-kinase-C enzyme and other related pathways. NF- $\kappa$   $\beta$  transcribes several proinflammatory cytokines.<sup>(8)</sup>

It has also been reported that the n-6 PUFA levels in the serum are higher in periodontitis patients, suggesting that an imbalance between n-6 and n-3 fatty

acids may contribute to susceptibility to oral bone loss.<sup>(9)</sup>

The main functional value of pomegranate in oral health is its polyphenolic flavonoid content. The components of pomegranate juice were found to significantly inhibit cytokine IL-8, PGE<sub>2</sub>, nitric oxide, human salivary  $\alpha$ -amylase,  $\alpha$ -glucosidase activity and found to reduce aspartate aminotransferase activity in saliva. The hydro-alcoholic extract from pomegranate fruit has shown to decrease the Colony Forming Unit (CFU) per milliliters of dental plaque by 84%.<sup>(10)</sup>

The seeds of *Garcinia mangostana* are reported to contain vitamin C. A composition in the form of a biodegradable gel, chip or ointment is provided for the treatment of periodontitis, comprising an antimicrobial or antibacterial activity against periodontal pathogen and forms a liquid crystal structure on contacting gingival fluid, which releases active ingredients gradually, to provide a sustained release dosage form.

The effect of *Morinda citrifolia* L. fruit juice significantly mitigated the gingival inflammation. The combination of good oral hygiene and administration of this juice was a promising treatment for gingivitis and periodontitis because of its strong anti-inflammatory effects.

Researchers have demonstrated antioxidant depletion in periodontitis locally in the periodontium<sup>30</sup> and within plasma, where investigators established an inverse relationship between reduced concentrations of plasma total antioxidants and vitamin C and increased prevalence of periodontitis.<sup>(11)</sup> A rodent model of zinc deficiency has shown to have an increased susceptibility to periodontal disease progression, as revealed by increased plaque and higher gingival index measurements. As an example of the potential of nutrigenomics tool for assessing the role of nutrition in periodontal disease, the role of the micronutrient zinc, a zinc transporter gene and the risk of developing type 2 diabetes was investigated. Recent genome-wide association studies have identified a genetic-susceptibility locus for type 2 diabetes comprising a nonsynonymous single nucleotide polymorphism (C/T; rs13266634) in a  $\beta$  cell-specific zinc-transporter gene.

This zinc transporter gene (SLC30A8, coding for ZnT8) may be important in insulin storage and release.<sup>(12)</sup>

The recommendations of 2011 European Workshop on Periodontology suggested that the dental team should consider including fish oils, fibre, fruits and vegetables and to reduce levels of refined sugars as part of a periodontal prevention / treatment regime and a general health benefit message.<sup>(13)</sup>

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