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# LAB®-TEST 3: GENETIC SUSCEPTIBILITY IN PERIODONTAL DISEASE

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Periodontitis is a multifactorial disease in which both environmental and genetic factors play a role.

The role of bacteria in the initiation of periodontal disease is necessarily primary, however, a range of host related factors influence the clinical presentation and rate of progression of disease (1). The disease seems polygenic, and between clinically homogeneous patient groups, heterogeneity exists in polymorphic genes that may play a role (2). This means that there may be considerable variation among individuals in their risk for disease progression.

Most genetic research in periodontitis has focused on gene polymorphisms that play roles in immunoregulation or metabolism, such as cytokines, cell-surface receptors, chemokines, enzymes and others that are related to antigen recognition. Accordingly, some forms of variation in the genetic code may result in either altered expression or in functional changes of the encoded molecules, therefore perhaps making individuals with aberrant genotypes more susceptible to a given disease, or resulting in an increase of disease severity (3). Polymorphisms in the promoter region of genes can modify and altering the level of specific proteins expression that may cause significant changes in function (4, 5).

In particular, polymorphisms in genes encoding molecules of the host immune defence system, such as cytokines, have been targeted as potential genetic markers (2, 6).

Cytokines are key factors that mediate the inflammatory process during periodontal disease. They have a role in B-cell activation, proliferation and differentiation that are the majority of infiltrating cells in advanced periodontitis lesions (7). Thus, these variations can interfere with the progression of disease (8) because may be responsible for the repeated cycles of tissue inflammation observed in these disorders (9).

In periodontal disease periodonto-pathogenic bacteria accumulated in the subgingival region are the environmental factors that influence the inflammatory response in periodontal tissues (10). However, cytokines are considered to indirectly contribute to connective tissue destruction and bone resorption (11).

The recent literature, has been recognized in some predisposing gene polymorphisms the development of aggressive forms of periodontal disease, even in people who have excellent oral hygiene habits and relative scarcity of pathogenic bacteria. IL-1A, IL-1B, IL-10, IL-6 and COX2 are the most frequent genes associated with periodontal disease

IL-1 is a potent pro-inflammatory agent that is released by macrophages, platelets and endothelial cells. The gene encoding this cytokine is assigned to chromosome 2q13–21 (12). In the investigation by Kornman et al. (13), the IL-1 composite genotype (allele 2 of the IL-1A gene at position - 889 and allele 2 of the IL-1B gene at position + 3953) was identified as a severity factor in periodontitis, only among non-smokers.

Other study have demonstrated that variations in the IL-1A gene at position +4845 and the IL-1B gene at position +3953 are associated with increased susceptibility

*Key words: Polymorphism, genes, periodontal diseases, inflammation, bone, resorption*

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to severe periodontitis (12, 14).

Regarding the IL-6 gene it was demonstrated to be localized in chromosome 7p21. It appears that IL-6 gene polymorphisms affect the serum levels of circulating IL-6, and consequently modify the patient's response to periodontal treatment.

Nibali et al. demonstrated an association between IL6-174 GG genotype and the detection of periodonto-pathogenic bacteria like *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* in aggressive and chronic periodontitis, indicating the influence of genetic factors on the subgingival microbiota (15, 16).

Moreover, although the polymorphism (-1087) G/A locus on chromosome encoding interleukin-10 (IL-10) 1q31–32 isn't associated with chronic periodontitis susceptibility in Japanese and Brazilian subjects, it has shown to be linked to chronic periodontitis severity in Swedish Caucasians.[12]

Another study showed that the interleukin-10 promoter haplotype, ATA, is a putative risk indicator for aggressive periodontitis in German Caucasians (17).

Reichert et al. demonstrated that that IL10-592 SNP is functional in chronic periodontitis, being associated with lower levels of IL-10 (18).

IL-10 seems to attenuate periodontal tissue destruction through the induction of tissue inhibitors of metalloproteinases and the inhibitor of osteoclastogenesis osteoprotegerin. Lower levels of IL -10 consequently influence periodontal disease outcome.

Another gene implicated in the inflammatory periodontitis response is the cyclooxygenase-2 (COX-2), This gene is responsible for prostaglandin synthesis, an important mediator of tissue destruction in periodontitis.

COX-2 polymorphisms -1195GA and -765GC have been reported to be associated with periodontitis in populations of Taiwanese and Chinese ethnicity (19, 20). These results were confirmed by another study in a large sample of European patients affected by periodontitis (21).

Our laboratory (LAB® s.r.l., Codigoro, Ferrara, Italy) developed a genetic test that analyzes specific polymorphism of the genes above described, using PCR-Real time (Fig. 1).

Disease-associated genetic polymorphisms may reveal which elements within a complex network of proteins are critical in determining the risk and the severity of disease and would be valuable in therapeutic intervention on individualized approaches and preventive strategies of the development of periodontitis.

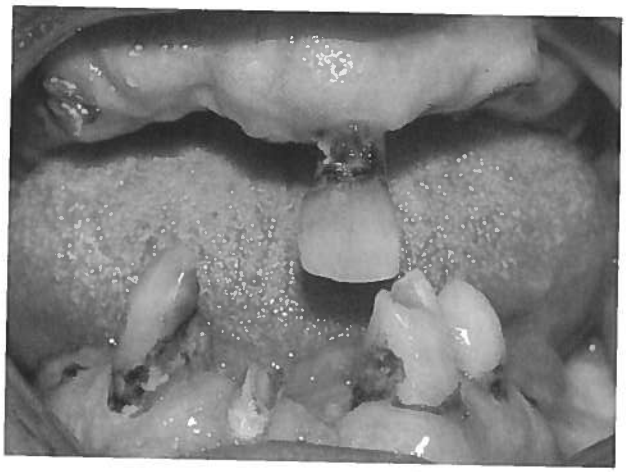

**Fig. 1.** *Periodontitis*

**Fig. 2.** *ABI PRISM 7500 (Applied Biosystems)*

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