

## Genetics and Caries – Prospects\*

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**Abstract:** Caries remains the most prevalent non-contagious infectious disease in humans. It is clear that the current approaches to decrease the prevalence of caries in human populations, including water fluoridation and school-based programs, are not enough to protect everyone. The scientific community has suggested the need for innovative work in a number of areas in cariology, encompassing disease etiology, epidemiology, definition, prevention, and treatment. We have pioneered the work on genetic studies to identify genes and genetic markers of diagnostic, prognostic, and therapeutic value. This paper summarizes a presentation that elaborated on these initial findings.

**Descriptors:** Dental Caries; Genetics; Genes.

### Summary of the presentation

Although there is growing evidence that genetics contributes to caries, historically, there has been a lack of studies addressing the problem from this angle. Caries is the consequence of the interaction of host factors, microbial infection, and substrate-favoring cariogenic microbiota. It is not difficult to propose underlying genetic mechanisms modulating each of these factors, such as saliva factors, which influence bacterial adhesion or acidic buffer capacity.

When looking at models that can incorporate genetic influences, it is important to consider the facts. In regard to types of diet and sugar consumption, a decline in caries experience based on DMFT/dmft scores in the past 5 decades in the US can be observed despite the very high sugar intake of the population.<sup>1,2</sup> This decline is likely due to measures such as school-based education programs and fluoride exposure. In general, promoting dietary changes alone has little or no impact on the future caries experience of the population. Water fluoridation also showed an effect on caries experience in the US in the same period, with a decline in DMFT scores. However, not all individuals living in fluoridated areas experienced lower disease rates, suggesting fluoride alone is not enough to protect everyone.

Human models, including studies with twins, provide evidence that caries involves a genetic component. The classic Vipeholm study<sup>3</sup> clearly showed that greater exposure to foods rich in sugar increased the severity of caries, but although the individuals in the study consumed caramels four times a day in between meals, 20% of them had not developed any caries lesions after one year. This result suggests that individual susceptibility also modulates caries experience. Only one publication related to the Vipeholm study looked at familial aggregation related to caries, and

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it showed that parents and siblings of subjects of the Vipeholm study who did not develop any caries lesions had significantly lower caries prevalence than the parents and siblings of the remaining subjects.<sup>4</sup> Twin studies also provide evidence that genetics influences caries. Several variables related to caries experience (i.e. number of teeth present, percentage of teeth restored, percentage of surfaces restored, percentage of teeth affected by caries, percentage of surfaces affected by caries) show statistically significant concordance rates in monozygotic twins, but not in dizygotic twins.<sup>5</sup> These studies measure heritability, or the amount of variation in the disease frequency that is due to genetic variation, and twins have been studied in the US, Brazil, and China, with heritability values ranging from 25% to 80%, depending on the disease-related variable studied.

Animal models have also been used to investigate the genetic contribution to caries, particularly in Japan. The basic design of this approach involves crossing strains particularly susceptible to the disease with resistant strains. It has been suggested that loci in chromosomes 1, 2, 7, 8, and 17 contribute to caries susceptibility.<sup>6-8</sup>

Our studies of the genetic contribution to caries involve two study designs:

- candidate-gene approaches and
- genome-wide scan approaches.

Since caries is influenced particularly by the environment (oral hygiene habits, types of diet, fluoride exposure, access to care), the main emphasis of our group was to characterize the study population in order to decrease heterogeneity. We observed that a collection of about 100 dry skulls derived from individuals that lived in the northeast of the United States more than 100 years ago had high caries

experience, but not all specimens had signs of the disease.<sup>9</sup> These individuals lived in times prior to organized dentistry, and most likely had the same oral hygiene practices and dietary habits as the general population. Since we have access to population samples from many areas, we decided to focus on groups with limited access to dental care and information about oral health. We performed the first genome-wide linkage studies on caries in a group of families from the Philippines. These families lived in rural areas and had similar cultural and behavioral habits. We detected a suggestive linkage between low caries experience and loci 5q13.3, 14q11.2, and Xq27.1. Moreover, high caries experience was linked to loci 13q31.1 and 14q24.3.<sup>10</sup> The candidate-gene approaches include three main groups of genes:

- genes involved in enamel development,
- in saliva formation and composition, and
- in immune response.

These studies include populations from Tiquisate, Guatemala, Istanbul, Turkey, Pittsburgh, USA, and the Patagonian region of Argentina. All these populations have similar socioeconomic status and access to dental care. Initial results are very encouraging and suggest associations can be found between these candidate genes and high caries susceptibility.<sup>11-13</sup>

## Conclusion

In summary, we believe genetic susceptibility to caries can be identified under specific experimental conditions. Several genes most likely influence individual susceptibility to caries, and these include genes involved in enamel development, in saliva function, and in immune response.

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