Defining the Contribution of Genetics in the Etiology of Dental Caries

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INVITED EDITORIAL

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Defining the Contribution of Genetics in the Etiology of Dental Caries

Dental caries is a highly prevalent disease that is disproportionately distributed in the population. The etiology is complex and multifactorial, with contributions from nutrition, tooth morphology, fluoride exposure, microbial ecology, salivary flow, oral hygiene, and other factors that remain to be defined. The magnitude each of these factors contributes to caries can vary significantly on an individual basis. The relative contributions of genetics and environment in each of these domains have not been defined (Shuler, 2001). In the current issue of the Journal, Wendell et al. report on the association of genetic variations in taste pathway genes and dental caries. They evaluated non-synonymous SNPs in the taste pathway genes TAS2R38, TAS1R2, and GNAT3 and their association with caries variation in an Appalachian population. This interesting study provides insight into the methodology that will allow for dissection of the nature vs. nurture issue in the etiology of dental caries.

The role of genetics in caries etiology has been investigated by a variety of approaches since the early 1900s, with twin studies providing convincing evidence that variations in risk and protection against dental caries have a strong genetic component (Bachrach and Young, 1927; Goldberg, 1930; Conry et al., 1992; Brez et al., 2005). Traits such as tooth morphology (Sofaer, 1982; Garcia-Godoy, 1983), immune response (Cole et al., 1977; Lehner et al., 1981), saliva (Mandel et al., 1965), and diet contribute to the genetic determination of dental caries. Only a few specific genes have been associated with caries risk. For example, genes involved in enamel formation, including amelogenin, ameloblastin, and tuftelin, have been associated with dental caries (Slayton et al., 2005; Deelely et al., 2008; Patir et al., 2008). Our understanding of the specific genetic contributions of these traits to dental caries is now being studied by powerful post-Human Genome Project approaches such as those used in the study by Wendell et al. (2010).

Diet is often considered to be a strong environmental etiological factor for dental caries, with investigations of diet and dental caries focusing on the type and frequency of carbohydrate consumption. However, an individual’s genetic constitution in determining one’s preference for consuming carbohydrates has long been thought to be a potentially important risk factor for the development of caries (Shaw and Murray, 1980). The human gustatory system can sense four basic taste qualities, bitter, sweet, salty, and sour. The role of taste sensitivity and the ability to taste sweet and its role in the risk of developing dental caries have been evaluated by numerous investigators (Catalanotto and Keene, 1974; Catalanotto et al., 1979; Nilsson and Holm, 1983). More recently, studies examining genetically determined taste sensitivity to 6-n-propylthiouracil showed that individuals with low taste sensitivity experience a lower dental caries risk than those with high tasting sensitivity (Lin, 2003; Rupesh and Nayak, 2006). The study in this issue by Wendell et al. evaluates genetic variation in taste pathway genes, TAS2R38, TAS1R2, and GNAT3, and their relation to dental caries. The extent to which taste receptor specificity correlates with, or predicts, diet choice and diet-associated conditions such as obesity or dental caries is not known. The TAS2R38 gene is part of the TAS2R bitter taste receptor family (a family of 25 G protein-coupled receptors), and recent studies have shown that polymorphisms are associated with differences in bitter taste perception (Khataan, 2006). The study in this issue by Wendell et al. evaluates genetic variation in taste pathway genes, TAS2R38, TAS1R2, and GNAT3, and their relation to dental caries. The extent to which taste receptor specificity correlates with, or predicts, diet choice and diet-associated conditions such as obesity or dental caries is not known.

Interestingly, a significant association was found for certain alleles in the TAS2R38 that were protective from caries, while other haplotypes were associated with caries risk. This association held true only for the primary-dentition group that had a mean age of 3.4 years. There was no significant association in the mixed- and permanent-dentition groups, which had mean ages of 9.8 and 29.4 years, respectively. The TAS2R38 SNPs found to be protective for caries cause amino acid changes in the taste receptor that are associated with bitter sensitivity, or the so-called “supertasters” phenotype. Other alleles are associated.

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with decreased bitter sensitivity or insensitivity (non-tasters). As pointed out by Wendell et al. (2010), these findings suggest that these genetic variations could contribute to differences in dietary habits that influence the caries risk of these children. Future studies should include diet analysis to confirm or refute this. Evaluation of children classified with different tasting abilities has been associated with body weight and dietary habit differences (Keller and Tepper, 2004).

Powerful genetics approaches, such as genome-wide association studies (Vieira et al., 2008) on large populations, and the evaluation of genetic polymorphisms, such as presented in the study by Wendell et al. (2010), will ultimately provide the answer as to the specific contributions of genetics and the environment in the etiology of dental caries. These types of approaches are being used to investigate genetic differences in other potentially important players in the caries process, such as the acidic proline-rich salivary proteins or salivary buffering system (Zakhary et al., 2007; Peres et al., 2010). Additional approaches such as salivary proteomics are being used, and these too will advance our knowledge in this field (Zehetbauer et al., 2009). There currently exists evidence that genes associated with enamel formation, taste, and saliva contribute to caries risk and/or protection (Table). As new genetic variations are investigated and new approaches used, there is little doubt that additional genes will be identified that contribute to caries risk/protection. It seems quite plausible that the epigenetic factors such as DNA methylation, which is modified by environmental factors such as the intra-uterine environment and nutrition, could play a role in the genetic determinants of dental caries (Chmurzynska, 2010). A fundamental question remaining to be answered is the practical utility of clarifying the genetic vs. environmental components of the dental caries process. Will this knowledge translate into better targeting of specific interventions that would improve the oral or the general health of at-risk populations? Clearly, this is a laudable and likely achievable goal. Given that the majority of oral health care costs are directed at treating the ravages of dental caries, this line of research would seem appropriate.

**Table. Genes Contributing to Caries Risk or Protection**

<table>
<thead>
<tr>
<th>Process</th>
<th>Gene</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tooth development</td>
<td>Amelogenin (AMELX)</td>
<td>Patir et al., 2008</td>
</tr>
<tr>
<td></td>
<td>Ameloblastin (AMBN)</td>
<td>Patir et al., 2008</td>
</tr>
<tr>
<td></td>
<td>Tufelin (TUFT1)</td>
<td>Slayton et al., 2005</td>
</tr>
<tr>
<td>Salivary function</td>
<td>Acidic proline-rich proteins (PRH1)</td>
<td>Peres et al., 2010</td>
</tr>
<tr>
<td></td>
<td>Carbonic anhydrase 6 (CA6)</td>
<td>Zakhary et al., 2007</td>
</tr>
<tr>
<td>Diet/Taste</td>
<td>Bitter taste receptor [TAS2R38]</td>
<td>Wendell et al., 2010</td>
</tr>
<tr>
<td></td>
<td>Sweet taste receptor [TAS1R2]</td>
<td>Wendell et al. 2010</td>
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</tbody>
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**REFERENCES**


