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Commentary

Gene Phenotypes: The Role Can't Be Ignored in Etiology of Dental Caries

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Etiology of dental caries is crucial for disease prevention and cure. The traditional concept of dental caries is an imbalance in saliva defense, microbial load and life style habits like sugar consumption. Distinctions have been revealed between dental caries and caries-free microbiomes in terms of microbial community structure by DNA sequencing to elucidate and monitor supragingival plaque bacterial diversity in the primary dentition of young children (Aas et al., 2008; Xu et al., 2014; Teng et al., 2015). Xu et al. have found that caries-related genera included *Streptococcus* and *Veillonella*; while *Leptotrichia*, *Fusobacterium*, and *Porphyromonas* were more related to the caries-free samples. Interactions between the microbiome and sugar intake frequency were also found (Moynihan and Kelly, 2014; Tian et al., 2015). The bacterial community richness, diversity, structure, and relative abundance of bacterial taxa were significantly different between different levels of sugar consumption groups, and patients in the dental caries relapse group had higher sugar intake frequencies than those in the relapse-free group during follow-up. Also, distinct adhesion biotypes of *Streptococcus mutans* with increased cariogenicity were defined in a sample of Swedish adolescents (Esberg et al., 2017). Thus, both microbiome and clonal bacterial structures seems to be involved in plaque cariogenicity.

In *EBioMedicine*, Strömberg et al. combined specific human genotypes with susceptibility of dental caries, revealing the evidence of variation in specific human genes (Strömberg et al., 2017). PRH1 and PRH2 variation and adhesion of indigenous and cariogenic (*S. mutans*) model bacteria were measured in 452 12-year-old Swedish children along with traditional risk factors and related to caries at baseline and after 5-years. The children were grouped into low-to-moderate and high susceptibility phenotypes for caries based on allelic PRH1, PRH2 variation. The high susceptibility phenotype (Db, PIF, PRP12) suggests an autoimmune-like condition. Children had more caries despite receiving extra prevention and irrespective of eating sugar or bad oral hygiene or *S. mutans* infection, developing 3.9-fold more caries than P1 children from plaque accumulation in general when treated with orthodontic multibrackets; and had basic PRP polymorphisms and low DMBT1-mediated *S. mutans* adhesion.

Host-associated microbial communities are influenced by both host genetics and environmental factors. However, factors controlling the human oral microbiome and their impact on disease remain to be investigated. To determine the combined and relative effects of host genotype and environment on oral microbiome composition and caries phenotypes, Gomez et al. examine the supragingival plaque microbiome of 5- to 11-year-old twins and find that the early oral microbiome is shaped by both heritable and environmental factors. The most heritable oral bacteria were not associated with caries state, did not tend to co-occur with other taxa, and decreased in abundance with age and sugar consumption frequency. Thus, while the human oral microbiome composition is influenced by host genetic background, potentially cariogenic taxa are likely not controlled by genetic factors (Gomez et al., 2017).

As present etiological studies of dental caries focus on correlations between microbial load and life style habits, few studies have been done on the correlations between specific host genotypes, microbial load and caries, which is the highlight of this study by Strömberg et al. (2017). Host genotypes, microbiomes, life style, oral hygiene, and disease process may as independent influential factors have great potential to correlate with each other, contributing to the complex etiological network of dental caries. However, different genetic etiologies for caries may have differential networks of bacterial clonal and microbiome and other caries-related factors, while sharing such factors within the same caries etiology type.

As the study of Strömberg et al. used Swedish children and thus a genetically and culturally homogenous sample from a low prevalence population to identify different caries etiologies, broader extrapolation and universal application of the results in a clinical setting, will require expanding population race, age, and other demographic and etiology matching characteristics. Also, novel means for treatment of high risk individuals will be needed and low and high caries prevalence populations will have different needs.

The global economic burden of dental diseases amounted to 442 billion USD in 2010 and was 4.6% of global health expenditure (Listl et al., 2015). Dental caries can still not be detected until clinical symptoms arise but not by saliva, bacteria, or life style biomarkers, which do

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predict cross-sectional caries (Listl et al., 2015; Selwitz et al., 2007). Thus, new models to diagnose prevent, and treat dental caries based on etiology are needed. Variation in specific human genes, PRH1 and PRH2, that matches and predicts individual experiences with caries in children, suggests novel approaches for their diagnosis, prevention and treatment. It gives us a new perspective on dental caries etiology study, which is worthy of more attention in the future.

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Conflicts of Interest

The authors declare no conflicts of interest.

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