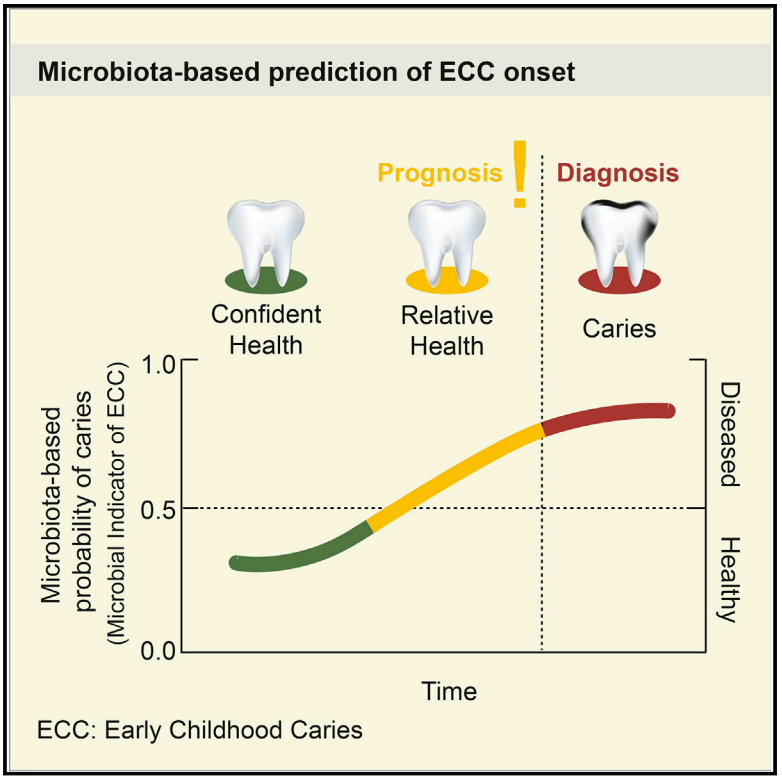
Article

Cell Host & Microbe

Prediction of Early Childhood Caries via Spatial-Temporal Variations of Oral Microbiota

Graphical Abstract



Highlights

- Oral microbiota in 50 four-year-old children were tracked for 2 years
- Age-dependent microbiota development is perturbed by early childhood caries (ECC) onset
- Shifts in microbiota precede manifestation of clinical symptoms of ECC
- Microbial Indicators of Caries, when de-trended for age, can predict ECC onset

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In Brief

Teng et al. tracked plaque and saliva microbiota of 50 4-year-old children for 2 years. By distinguishing between aging- and disease-associated taxa and exploiting the distinct microbiota dynamics between disease onset and progression, a predictive model, Microbial Indicators of Caries, is proposed as a method to predict future caries onset.

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Prediction of Early Childhood Caries via Spatial-Temporal Variations of Oral Microbiota

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SUMMARY

Microbiota-based prediction of chronic infections is promising yet not well established. Early childhood caries (ECC) is the most common infection in children. Here we simultaneously tracked microbiota development at plaque and saliva in 50 4-year-old preschoolers for 2 years; children either stayed healthy, transitioned into cariogenesis, or experienced caries exacerbation. Caries onset delayed microbiota development, which is otherwise correlated with aging in healthy children. Both plaque and saliva microbiota are more correlated with changes in ECC severity (dmfs) during onset than progression. By distinguishing between aging- and disease-associated taxa and exploiting the distinct microbiota dynamics between onset and progression, we developed a model, Microbial Indicators of Caries, to diagnose ECC from healthy samples with 70% accuracy and predict, with 81% accuracy, future ECC onsets for samples clinically perceived as healthy. Thus, caries onset in apparently healthy teeth can be predicted using microbiota, when appropriately de-trended for age.

INTRODUCTION

One key goal of human microbiome projects worldwide is to classify and predict host states based on human microbiota (Knights et al., 2011). The potential of microbiota-based classification of disease states has been tested in several studies such as plaque for gingivitis (Huang et al., 2014) and fecal samples for obesity (Le Chatelier et al., 2013), diabetes (Qin et al., 2012), and liver cirrhosis (Qin et al., 2014), etc. However, few studies have yet reported successful microbiota-based prediction of future disease outcome, especially for disease onset (Gevers et al., 2014). One explanation is that few experimental designs have simultaneously considered the spatial and temporal variation of microbiota during disease development. Along the temporal scale, microbiota change as the host ages, and their diversity and composition can change substantially due to the particular physiology, diet, and environmental exposure at a specific stage of host development (Song et al., 2013; Stahringer et al., 2012; Yatsunenko et al., 2012). For example, oral microbiota change during the normal aging process (Xu et al., 2015). On the other hand, at the spatial scale, microbiota from various physical niches (e.g., spatially distinct habitats such as the saliva and the plaque) can differ greatly in community structure (Costello et al., 2009; Huang et al., 2011; Huttenhower et al., 2012). Association of microbiota from multiple habitats with disease symptoms have been shown (Ling et al., 2010), although how the niches differed in their ability to model infections remained elusive.

Early childhood caries (ECC) is the most common oral disease in children. It affects approximately half of children worldwide and incurs enormous societal costs (Casamassimo et al., 2009). ECC leads to sustained demineralization of enamel and dentin, and the infection can spread from the affected tooth to the surrounding soft tissues, resulting in swelling and inflammation in highly progressed cases. Once started, the damage to teeth is irreversible, with child patients continuing to suffer from a higher risk for new lesions and even tooth loss over their entire lifespan (Chen et al., 2012; Leroy and Declerck, 2013; Selwitz et al., 2007). Therefore, preventive intervention of ECC is of particular clinical significance (Lancet, 2009; Selwitz et al., 2007). However, prediction of future ECC, particularly for new disease onset, has been difficult (Mejàre et al., 2014).

For the assessment of ECC risk, oral bacteria count (e.g., *Streptococcus mutans* count and salivary *Lactobacillus* count); chemical characteristics of saliva (e.g., buffering capacity and pH), baseline caries status (host oral condition at the first oral examination), as well as personal oral hygiene (e.g., visible plaque levels), behavior, diet (e.g., sugar intake) or socioeconomic level, have been employed as single-predictors or variables in multivariate models (Mejàre et al., 2014). However, limitations of these existing methods are apparent (Tellez et al., 2013). (i) Most of these risk factors are subjective, prone to human bias and error, and are not satisfactorily reproducible among