

Immune deficiency explains rampant caries in some children

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Researchers at Umeå University in Sweden have made a novel discovery connecting genetic innate immunity deficiencies to rampant caries and increased risk of dental caries affecting about one in five children. The results could lead to a better way of identifying high-risk patients and treat their caries. The study has been published in the journal *EBioMedicine*.

In a five-year study, in which saliva and isolated bacterial strains from a large number of [children](#) was analyzed and the dental health monitored, the research group recently established that some high-risk children have a more virulent variant of the caries bacterium *Streptococcus mutans*. The same research group now shows that high-risk children also have genetic defects in innate and adaptive immunity, making them more vulnerable against oral bacteria and streptococci in general.

"Most people consider caries to be a lifestyle condition caused by bad eating- and oral hygiene routines that lead to acidic pH levels in the mouth, which in turn damage the enamel and promote the colonization of acid-producing bacteria such as *S. mutans*," says Nicklas Strömberg, professor and Head at the Department of Cariology at Umeå University and Västerbotten County Council, and first author of the article.

"Our results now show that this correlation is accurate for approximately four out of five [individuals](#), who have a small-to-moderate risk of developing caries because their composition of salivary innate immunity proteins make them relatively resistant to caries. However, we have

shown that so-called high-risk individuals, which are about one in five individuals, carry a genetically different composition of the same salivary innate immunity proteins, making them highly susceptible to caries independent of eating- or oral hygiene habits or *S. mutans*-infection."

One in five children in Sweden is considered a high-risk individual when it comes to the risk of developing [dental caries](#). These high-risk individuals do not respond to traditional caries prevention or treatment, and bio markers cannot predict future risk of caries in the group. Chronic caries infection and missing teeth are also risk factors for systemic diseases such as stroke and cardiovascular diseases.

Innate and adaptive immunity deficiencies explain high-risk individuals for caries

A research group led by Nicklas Strömberg have in the current study followed 452 children (between ages 12 and 17) in Västerbotten over a five year period. After genetic analysis of their DNA, the children were divided into various risk groupings based on genetic variation in PRH1 and PRH2, encoding salivary acidic proline-rich proteins. At a five-year follow-up, the researchers could see how caries had developed in the various risk groupings.

The results showed that children with high susceptibility or risk for caries had defective proteins in their saliva. The defective salivary proteins in question were acidic and basic proline-rich proteins and the adhesive [protein](#) salivary agglutinin (or DMBT1). According to the researchers, the defective proteins probably fail to mediate the same innate and adaptive immunity responses that serve to protect individuals with small-to-moderate caries risk from the oral bacterial flora.

The researchers describe how allelic variation in PRH1 and PRH2,

encoding acidic proline-rich proteins, separate children into different caries susceptibility or risk groupings. As expected, children with a low-to-moderate susceptibility or risk for caries along with a genetically intact set of proteins were found to develop caries from bad eating and oral hygiene routines and *S. mutans*-infection. However, the children with high susceptibility develop caries independent of eating- or oral hygiene routines or *S. mutans*-infection but from the immune deficiency. Accordingly, when children were treated with dental braces the high risk children exclusively developed several times more caries after 5 years. The researchers believe this is due to plaque accumulation and impaired saliva flow as a result from the dental braces.

"This new knowledge about genetic susceptibility groupings could be used to improve individualized dental care. Children in the higher risk group could then be diagnosed before caries lesions and symptoms arise. In this way, prevention could be implemented at a young age when caries can be prevented more easily. High-risk children can presently be treated with intensified prevention and in the future we will hopefully be able to use immune-supplementation as a way to strengthen their oral immunity," explains Nicklas Strömberg.

Dental costs, including those pertaining to [caries](#) treatment, amount to 5 % of global health care-related costs. Caries is the most common cause for failure of fillings and prosthetic replacements. The ability to detect high-risk individuals early could yield large savings for society and individuals both in terms of suffering and costs.

More information: Nicklas Strömberg et al, Genetic- and Lifestyle-dependent Dental Caries Defined by the Acidic Proline-rich Protein Genes PRH1 and PRH2, *EBioMedicine* (2017). [DOI: 10.1016/j.ebiom.2017.11.019](https://doi.org/10.1016/j.ebiom.2017.11.019)

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