Diamond X-rays used to discover tooth decay enzymes

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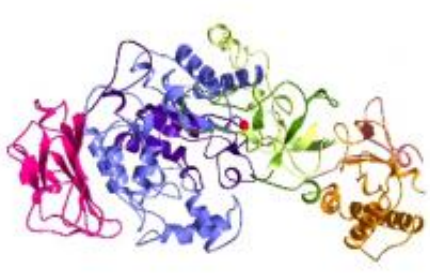
An artist's impression of a glucansucrase enzyme from the dental caries pathogen S. mutans forming a biofilm, and the acids within. Glucansucrase catalyses the formation of glucan (white, hexagonal chains) with various types of glucosidic linkages, from disaccharide sucrose (glucose + fructose). Then, the high-molecular sticky glucan adheres to tooth surfaces to form dental plaques, which can in turn cause additional infections, periodontal disease and halitosis. Reprinted from the Journal of Molecular Biology, Vol 408, Issue 2, Keisuke Ito et al. 'Crystal Structure of Glucansucrase from the Dental Caries Pathogen Streptococcus mutans'. Pages 177-378, Copyright (2011), with permission from Elsevier."

Scientists using Diamond Light Source have made a breakthrough in the battle against tooth decay, with research published in the leading *Journal of Molecular Biology* (JMB) on 29 April 2011.

Researchers from the UK and Japan used the Diamond synchrotron in Oxfordshire and the Photon Factory in Tsukuba city, Japan, to solve the 3D structure of an enzyme that plays a key role in tooth decay caused by sugar.

Tooth decay can occur when a biofilm, or dental plaque as it is more commonly known, is formed by a large and sticky glucose polymer called glucan. The glucan biofilm contains bacteria and food debris and forms on the surface of the tooth. As they grow, the bacteria secrete acids which break down the tooth's hard enamel on the surface. The structural information published in JMB provides a critical insight into how the enzyme 'GTF-SI', a glucansucrase, forms glucan, the sticky biofilm substance.

"With the use of the Diamond synchrotron and the Photon Factory we have been able to solve not only the structure of the enzyme alone but also its structure when bound to an existing inhibitor. Several inhibitors that prevent this type of enzyme forming glucan have been identified but to date there has been little structural information available. With the data we collected at Diamond and the Photon Factory, we now have a better understanding of how the enzyme functions and how it can be stopped. This structural information should be useful in the design of novel inhibitors that will prevent the biofilm formation by glucansucrases and reduce the risk of possible side effects such as hypoglycaemia. These novel inhibitors could be incorporated into toothpaste and mouthwash, making them more effective at preventing tooth decay," said Sohei Ito, Laboratory of Food Protein Engineering, University of Shizuoka in Japan, and lead researcher on the project.



Ribbon diagram showing the structure of glucansucrase from the dental caries pathogen S. mutans. Courtesy Sohei Ito, University of Shizuoka, Japan.

The structural data collection at the Diamond synchrotron was carried out on the I02 Macromolecular Crystallography (MX) experimental station. Principal Beamline Scientist, Professor Thomas Sorensen, says, “Knowing the 3D structure of the enzyme is like knowing the shape of a lock you need to find a key for – it makes it much easier to find the right key that will fit. In this case, the inhibitor acts like the key, fitting into the lock in just the right way so that it can do its job.”

Sweet is an important favourable taste quality linked to food intake in humans and sucrose, the most common form of sugar, is the most highly consumed sweetener. But sucrose causes tooth decay, or dental caries as it is known. According to the World Oral Health Report 2003, dental caries is a major health problem in most industrialized countries, affecting 60-90% of school children and the vast majority of adults. If left untreated for a long period of time it can result in pain and tooth loss, and can lead to additional infections, periodontitis (gum disease), halitosis (bad breath) and in some cases even death by sepsis. Novel inhibitors open up the potential of reducing the risk of tooth decay by preventing the formation of dental plaque.

Diamond Light Source produces the extremely intense X-ray beams required for looking at the molecular interactions involved in a variety of biological processes. Advances in structural biology have accelerated

greatly as a result of access to the synchrotron facilities that have been developed around the world in the past 25 years. Biologists have been swift to recognise the huge potential that lies behind understanding the multitude of processes that take place within living organisms at a molecular level. Researchers in the UK are at the forefront of this work and Diamond Light Source plays its part in providing cutting edge facilities for protein structure determination.

Diamond currently has five experimental stations dedicated to structural biology as well as an on-site Membrane Protein Laboratory. The work carried out at the synchrotron has the potential to affect our everyday lives. Previous breakthroughs using structural data from Diamond include gaining a better understanding of hypertension in the pre-natal condition pre-eclampsia, learning how a key tuberculosis drug is activated, understanding how bird flu can affect humans, and revealing the mechanism used by HIV to attack the body.

More information: 'Crystal Structure of Glucansucrase from the Dental Caries Pathogen Streptococcus mutans' Keisuke Ito, et al. *Journal of Molecular Biology*, Volume 408, Issue 2, Pages 177-378 (29 April 2011) dx.doi.org/10.1016/j.jmb.2011.02.028 ;

Provided by Diamond Light Source