Structural studies on the glucosyltransferases of *Streptococcus mutans*

Norbert Schormann¹, Ren Wu¹, Manisha Pate¹, Hui Wu² and Champion Deivanayagam¹

¹Department of Biochemistry and Molecular Genetics, University of Alabama at Birmingham), ²School of Dentistry, Oregon Health Science University

champy@uab.edu

**Keywords:** Glucosyltransferases, Dental Caries, *Streptococcus mutans*

Dental caries is a polymicrobial disease that affects much of the human population worldwide, where the harmony of a cooperative eco-organization among commensal microbes shifts towards a dysbiotic framework with an overrepresentation of pathogenic microorganisms, particularly by *Streptococcus mutans* (SM)[1-3][4]. The progression of the disease begins with bacterial attachment, and a complex cascade of events that include the production of soluble (1,6-linked) and insoluble (1,3-linked) glucans by glucosyltransferases (Gtfs) that belong to the GH70 hydrolase family. This class of enzymes utilizes dietary sucrose to produce various isomeric glucan polymers through two important steps: (i) first is the sucrase (invertase) activity, where cleavage of sucrose results in glucose and fructose; (ii) subsequently, the polymerization of glucose molecules forms extended α-glucans. The by-product of SM’s metabolic activity results in acidification of the local microenvironment on the tooth surface, eroding tooth enamel and eventually leading to the onset of dental caries[5-7]. *S. mutans* is a prolific producer of both soluble and insoluble glucans[1], where the insoluble glucans act as a glue bringing together biofilm communities, providing mechanical stability[8].

We have expressed purified and crystallized the GtfD (173-1476). High resolution data (2.2 Å) as collected at SERCAT-APS. Structure solution was carried out using molecular replacement. We will also present the co-crystallization of sucrose with a mutant enzyme, and co-crystallization with dextran (Figure 1). Through these structural studied, we have discovered a novel mechanism through which these enzymes synthesize these elongated glucans. Developing inhibitors to this enzyme is a priority, as it directly affects biofilm formation with the dysbiotic oral microbiome.

**References:**