Abstract (300 words)

Prader-Willi Syndrome (PWS) is a genetic disorder caused by the lack of expression of certain paternal genes, which normally causes cognitive, neurological and endocrine abnormalities. PWS patients have low salivary flow with acidic salivary pH compared with their healthy peers. Hyposalivation are always associated with increased dental caries; however, the caries prevalence of PWS patients doesn't appear to be higher. In the oral cavity, arginine and proteins containing arginine are primarily catabolized by the arginine deiminase system (ADS) present in oral arginolytic bacteria. The ammonia generated by the ADS elevates biofilm pH, which prevents the loss of tooth mineral. Several clinical studies have demonstrated the reverse correlation between caries rate and ADS activities. PWS patients have several folds of total salivary protein concentration and normal total output of salivary proteins compared with non-PWS controls. Therefore, we hypothesize that normal salivary protein output helps maintain the homeostasis of oral biofilms in PWS patients. To test this hypothesis, a cross-sectional clinical study is proposed. Based on a power analysis, thirty subjects (PWS patients:Controls=1:1, aged from 5 to 18 year-old*) will be recruited. The IRB protocol has been submitted and is currently under review**. Aim 1 will determine the total output of salivary proteins and the proteomic characteristics of the saliva. Aim 2 will determine the ADS activities and the microbiome characteristics of the oral biofilms. The microbial composition variation will be analyzed by Amplicon Sequence Variants (ASVs) 16S rRNA sequencing analysis. Linear regression analysis will be used to evaluate the statistical associations of the ADS activities, salivary protein total output, and microbiome data. These critical preliminary data will be used for a larger scale NIH R01 grant to explore the mechanisms of caries prevention in PWS patients. The long-term goal is to develop innovative modalities or reagents to protect high-risk patients from dental caries.

**Seattle Children's Hospital has a PWS Clinic (www.seattlechildrens.org/clinics/prader-willi-syndrome-clinic) where subjects will be recruited*

IRB application has been submitted to Seattle Children's Hospital:* ***IRB code (STUDY00005278: PWS Oral health, *and expected to be approved in early 2025*