Identification and validation of DNA methylation biomarkers for [Bardet-Biedl Syndrome (BBS)](https://www.marshfieldclinic.org/services/bardet-biedl-syndrome)

**Research Goal**

The overarching goal of this study is to discover DNA methylation profile and genetic-DNA methylation interaction that contribute to Bardet-Biedl Syndrome (BBS). Bardet-Biedl syndrome (BBS) is a rare genetic disorder (1 in 140,000) present from birth that affects many parts of the body. Bardet-Biedl Syndrome had originally been thought to be a recessive disorder, however, recently compound heterozygosity mutation was also demonstrated to be pathogenic. Currently, there is no any research have been conducted to BBS. We hypothesis DNA methylation may play roles in BBS or have corresponding adaption to BBS specific disease genetic variations.

**Specific Aims**

**Aim 1:** To generation whole genome DNA methylation profile for Bardet-Biedl syndrome with genome-wide bisulfite sequencing and methylation microarray. We plan to identify all the differential methylation regions in BBS and investigate the causal or consequential roles of DNA methylation in the pathology of BBS. Meanwhile, we will compare the methylation difference between different tissues including PBMC, CD4+ T-cell, CD8+ T-cell, salivary cells.

**Aim 2:** To investigate the influence from genetic variation of Bardet-Biedl Syndrome (BBS) to DNA methylation architecture. Bardet-Biedl syndrome is a genetically heterogeneous ciliopathy, we plan to exploit the epigenetic difference between different Bardet-Biedl Syndrome (BBS) genetic background.

**Aim 3:** To identify potential salivary based DNA methylation diagnostic and risk prediction biomarker for Bardet-Biedl Syndrome (BBS). Genetic pathogenic variants could only provide the disease risk, however, it cannot be used to predict the time of disease onset. We plan to identify DNA methylation biomarkers which can be used for recent event warning for the patients.

Currently, there is no any DNA methylation reference for BBS. We will provide the first DNA methylome reference for BBS which will provide a comprehensive resource for future epigenomic research to BBS.

**Background**