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Final Project Abstract

The group that I’m currently working on my master’s thesis with are interested in studying the effect of early diet exposures on changes in methylation in type 1 diabetes (T1D). They have collected DNA methylation measurements from peripheral whole blood at up to five timepoints for 87 cases and 87 frequency-matched controls. Of these, approximately 120 participants also have early diet data, which includes information about breast feeding, gluten introduction, etc. Participants were randomly assigned to either the 450K or EPIC methylation array platforms, with 184 samples from 84 subjects profiled on the 450K platform and 211 samples from 90 subjects profiled on the EPIC platform.1 The group has already done a huge amount of work preparing the data, and data from both platforms has gone through the SeSAMe pipeline2 which includes Noob normalization, non-linear dye bias correction, and pOOBAH for probe detection above background. So, data cleaning and preparation should be fairly minimal for this analysis. In order to test whether early diet is associated with longitudinal changes in methylation positions, I will use linear mixed models that include terms for T1D status and an early diet variable of interest. This will involve some careful model selection, because we will likely need to adjust for other clinically relevant variables such as age and sex. Also, it will be interesting to see if there is an interaction effect between T1D status and early diet variables. I hope to do this analysis in a fairly untargeted way (looking at all probes and early diet variables), but it’s possible that this will take too much time. If this is the case, I will focus on infant diet variables that have been previously associated with differential methylation in T1D, such as gluten introduction. Hopefully we will find methylation positions that are longitudinally associated with early diet, and ideally these methylation sites will have some sort of biological association with T1D (for example a known association with gene expression in pancreatic cells).

References

1. Johnson RK, Vanderlinden LA, Dong F, et al. Longitudinal DNA methylation differences precede type 1 diabetes. *Sci Rep*. 2020;10(1):3721. doi:10.1038/s41598-020-60758-0

2. Zhou W, Triche TJ, Laird PW, Shen H. SeSAMe: reducing artifactual detection of DNA methylation by Infinium BeadChips in genomic deletions. *Nucleic Acids Res*. 2018;46(20):e123-e123. doi:10.1093/nar/gky691