MS Thesis Proposal

Tim Vigers

Abstract

Introduction

Type 1 diabetes (T1D) is an autoimmune disease characterized by the production of antibodies which target pancreatic -cells. This leads to both micro and macrovascular complications, and individuals with T1D are at an increased risk of experiencing a major cardiac event (e.g. stroke, angina, and myocardial infarction) and are less likely to have satisfactory outcomes after a coronary event.1 The disease currently affects over 30 million people worldwide,2 and is increasing by 3-4% per year on average.3 However, the global burden of disease is difficult to estimate due to geographic variation in incidence1,3.

Although genetic predisposition accounts for some of the etiology of T1D (sibling relative risk has been estimated at 154), geographic variation in incidence, low monozygotic twin concordance (approximately 50%), and studies of migrant populations suggest that non-genetic factors also play an important role in T1D development2.

Metabolites are small molecule products of metabolism, and are involved in many vital processes, including energy storage, cellular signaling and apoptosis, post-translational protein modification and transport, and maintenance of homeostasis in the cellular milieu5. Analysis of the metabolome can therefore quantify the integrated response to endogenous and exogenous disease factors or other physiological changes. Previous studies have found an association between T1D and changes in phospholipids and sphingolipids and excretion of modified amino acids6.

References

1. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. *The Lancet*. 2014;383(9911):69-82. doi:10.1016/S0140-6736(13)60591-7

2. Rakyan VK, Beyan H, Down TA, et al. Identification of Type 1 Diabetes–Associated DNA Methylation Variable Positions That Precede Disease Diagnosis. *PLOS Genet*. 2011;7(9):e1002300. doi:10.1371/journal.pgen.1002300

3. Tuomilehto J. The Emerging Global Epidemic of Type 1 Diabetes. *Curr Diab Rep*. 2013;13(6):795-804. doi:10.1007/s11892-013-0433-5

4. Polychronakos C, Li Q. Understanding type 1 diabetes through genetics: advances and prospects. *Nat Rev Genet*. 2011;12(11):781-792. doi:10.1038/nrg3069

5. Johnson CH, Ivanisevic J, Siuzdak G. Metabolomics: beyond biomarkers and towards mechanisms. *Nat Rev Mol Cell Biol*. 2016;17(7):451-459. doi:10.1038/nrm.2016.25

6. Frohnert BI, Rewers MJ. Metabolomics in childhood diabetes. *Pediatr Diabetes*. 2016;17(1):3-14. doi:10.1111/pedi.12323