Epigenetics of Skin Intrinsic Florescence

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Received May 15, 2020

Accepted for publication June 1, 2020

Published online September 26, 2021

Abstract

Introduction: Cumulated advanced glycation end products (AGEs) in the bloodstream and tissues contribute to the pathogenesis of diabetes complications. The skin intrinsic fluorescence (SIF) is a non-invasive measurement of dermal AGEs level using spectrometer, and it can be used as a biomarker in AGEs-related diseases. Previously, specific epigenomic factor has been found to be associated with haemoglobin A1c (HbA1c). HbA1c is a type of glycated haemoglobin – the HbA1c test measures the average glycemic control over the period of 3 months. However, the effect of epigenetic factors on the level of AGEs in the skin remains unknown. We hypothesize that some cytosine-guanine dinucleotides (CpGs) are associated with SIF. An epigenome-wide associations study (EWAS) was performed to identify CpG sites associated with SIF in people with type 1 diabetes.

Methods: 499 people with type 1 diabetes that have both methylation and SIF from the Diabetes Control Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study were included. We fit linear regression models for SIF with each CpG site one at a time. The epigenome-wide significance level ($p=5e-8$) was applied. Then the result is compared with the null hypothesis where CpGs are not associated with SIF to check the inflation. In order to check the assumptions of the multiple linear models at a single CpG, we use diagnostic plots.

Results: We did not identify a specific CpG that is significantly associated with neither skin intrinsic fluorescence 1 (SIF1) nor skin intrinsic fluorescence 12 (SIF 12). The CpG site with strongest effect is cg06538183 ([SE] -2.73 [0.61], $p = 8.72e-6$) on SIF1 and cg12871967 ([SE] 2.52, 0.53, $p = 2.71e-6$) on SIF12.

Conclusion: We did not find any specific CpG that was significantly associated with either SIF 1 or SIF12. In general, the result suggests that DNA methylation does not impact the accumulation of AGEs in skin cells. DNA methylation data has a unique pattern of distribution that drives the non-uniform distribution of the p-values. The group of 275,301 CpGs that have means above the median and standard deviations below the median has the expected uniform p-value distribution.