Genome-wide investigation of DNA Methylation in peripheral T-cells from patients with CAH

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Introduction

Patients with CAH (21OHD) are at risk of long term cognitive and metabolic sequelae. DNA methylation may be a possible mechanism which mediates long term outcome in patients.

Objective

To investigate genome-wide methylation in patients with CAH in order to find evidence for genomic reprogramming which may mediate long term outcome.

Methods

CD4+ T-cell DNA from 28 patients with CAH (18.5±6.5 yrs) and 37 population controls (17.0±6.1 yrs) were analyzed with the Infinium HumanMethylation450 BeadChip array (450K array) to measure genome-wide locus specific DNA methylation. Effects of CAH (phenotype and genotype) on methylation were investigated as well.

Results

Patient phenotype correlated with two CpG sites: cg18486102 (rho=0.58, p=0.027) and cg02404636 (rho=0.58, p = 0.038). cg02404636 also correlated with genotype (rho = 0.59, p = 0.024). The level of methylation (β-values) for both differentially methylated probes (DMP) are shown in Figure 2. cg18486102 is located in the TSS region of the genes, to be associated with the severity of the disorder and cg02404636, to be associated with the severity of the disorder and FAIM2 gene and cg02404636 in the TSS1500 region of the gene.

Conclusions

This is the first analysis of genome-wide DNA methylation in patients with CAH. We identified two CpGs, cg18486102 and cg02404636, to be associated with the severity of the disorder and CYP21A2 genotype. The CpGs were located in the TSS region of the genes FAIM2 and SF11, respectively. Both genes are biologically relevant considering the long term metabolic and cognitive outcome in patients with CAH.