

## Poster Number 45

### Abstract 0240\_0346\_000070

#### Altered methylation of promoters in genes involved in inflammatory and metabolic pathways in First Nations adolescents with type 2 diabetes

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#### Background:

Type 2 diabetes (T2D) is increasing in adolescents. DNA methylation is a cellular process by which methyl groups are added to DNA molecules, regulating gene expression. Obesity may be associated with T2D but Indigenous populations are disproportionately affected by this complication and the cause is unknown.

#### Objective:

We hypothesize that DNA methylation patterns of genes associated with obesity and T2D risk are altered in First Nations adolescents diagnosed with T2D.

#### Methods:

Peripheral blood mononuclear cells (PBMCs) were obtained from a prospective cohort of First Nations adolescents diagnosed with T2D (n=21) and the majority of whom are obese (the iCARE cohort) and the controls (n=10). All samples were sequenced using SOLiD. Data were analyzed using diffReps with a 200bp window size and the Negative Binomial test to identify differentially methylated regions (DMRs). A false discovery rate  $\leq 0.05$  and fold change  $\geq 1.5$  were used as cut-off parameters.

#### Results:

565447 DMRs were identified in PBMCs from T2D patient samples compared to controls. DNA from the PBMCs of First Nations adolescents with T2D were hypomethylated compared to controls. We identified several novel DMRs, of which 1110 were found in the gene promoter region. These gene promoter region DMRs included those associated with pro-inflammatory and metabolic pathways, including; glycoprotein hormones, alpha polypeptide (CGA), janus kinase 2 (JAK2), interleukin 5 (IL5), and glutamate-ammonia ligase (GLUL), glutamyl-tRNA amidotransferase subunit B (GATB), glutaminase 2 (GLS2), U2 small nuclear RNA auxiliary factor 2 (U2AF2) respectively.

#### Conclusion:

Differences were observed in the DNA methylation pattern of PBMCs from First Nations adolescents diagnosed with T2D when compared to controls. Differential methylation of promoters in genes involved in inflammatory and metabolic pathways could play a crucial role in defining T2D risk in First Nations adolescents.