

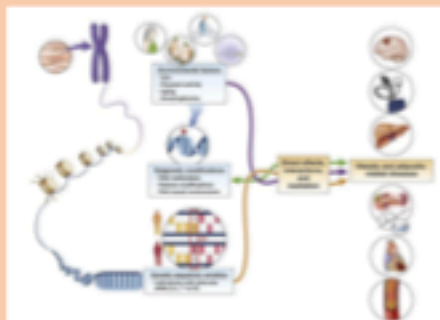
A genome-wide methylation study of body fat traits in the Norfolk Island Isolate

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Introduction

- Obesity is a complex disorder that increases the risk of many end-stage diseases (e.g. diabetes, heart disease).
- Obesity is influenced by both genetic and environmental factors.
- Epigenetic variation may mediate the interaction of these factors



Study Objectives

The aim of this research is to identify epigenetic markers associated with body fat traits in a healthy cohort. In this poster, the results from cross-sectional study of all samples is provided.

Methods

The study was performed on the cohort of 48 healthy adults with following methods:

- ❖ Body fat traits:
 - body fat percentage (BF)
 - Body mass index (BMI)
 - Hip circumference (HC)
 - Waist circumference (WC)
 - Waist-hip ratio (WHR)
 - Weight (W)
- ❖ Genome-wide DNA methylation measured using Illumina 450K from whole blood samples
- ❖ Statistical analysis was performed using custom R scripts including the MINFI package to identify differentially methylated positions (DMPs) associated with each trait.

Results

Table 1: Significant DMPs associated with body fat traits

Trait	CpG	Chr	Position	Gene	beta	P-value†	Region
PC1	cg04946709	16	59789030	GOT2-CDH8	↑	3.19×10^{-6}	Body
BW	cg04946709	16	59789030	GOT2-CDH8	↑	5.83×10^{-6}	Body
HC	cg22455090	5	89825803	LYSDM3	↑	1×10^{-7}	TSS1500
PC2	cg22538323	7	27702700	HIBADH	↑	1.17×10^{-7}	TSS200
HC	cg16379671	12	131647826	ADGRD1	↑	2.02×10^{-7}	
BMI	cg26576937	20	2739938	EBF4	↑	2.08×10^{-7}	3'UTR

† adjusted for covariates

BW = Body Weight HC= Hip Circumference BMI= Body Mass Index

Table 2: Pathways associated with body fat traits

ID	Name	P-value	P_{adj}^*	Genes In list	Total Genes
P00012	Cadherin signalling pathway	3.23×10^{-10}	6.76×10^{-7}	28	159
P00057	Wnt signalling pathway	7.44×10^{-9}	7.78×10^{-6}	38	305
946598	Thyroid hormone signalling pathway	5.1×10^{-5}	2.82×10^{-2}	16	116
692234	PI3K-Akt signalling pathway	5.39×10^{-4}	2.82×10^{-2}	32	342
1268881	Constitutive Signalling by AKT1 E17K in Cancer	7.75×10^{-5}	3.25×10^{-2}	7	25
M295	Genes related to PIP3 signalling in cardiac myocytes	1.58×10^{-4}	4.79×10^{-2}	11	67
868086	Rap1 signalling pathway	1.6×10^{-4}	4.79×10^{-2}	22	210

* Benjamini-Hochberg adjusted P-value

Conclusions

By investigating a healthy cohort of individuals, we have identified:

- Five significant DMPs, which mapped to *GOT2-APOOP5-CDH8*, *LYSDM3*, *HIBADH*, *ADGRD1* (*GPR133*)-*LINC01257* and *EBF4* genes
- Two significant pathways (Cadherin signalling and Wnt signalling) associated with body fat traits

Overall, this study provides new insights into epigenetically-influenced mechanisms underlying body fat variation in a healthy cohort, which could be considered targets for studying obesity in future studies