An investigation into the DNA methylation patterns of risk and time preference in older individuals

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Problem / Question

How do risk and time preferences for a group of individuals associate with their epigenetic methylation profile?

Project Overview

- Time and risk preference are related to health behaviours, health and wellbeing outcomes and health inequalities
- Data was ascertained from the Northern Ireland COhort for the Longitudinal study of Ageing (NICOLA)
- 8,452 participants were recruited as part of NICOLA
- Risk preferences were established by asking participants to make a series of choices between two hypothetical income scenarios
  - Data was collected for 4,564 individuals
- Time preferences were determined by asking participants to make choices between a series of hypothetical scenarios
  - Data was collected for 4,585 individuals
- Blood-derived DNA was analysed using the Infinium HD Methylation Assay, MethylationEPIC BeadChips from Illumina
- The status of >850,000 CpG sites, promoters and CpG islands was evaluated
- We compared the distribution of single site DNA methylation levels between *risk averse* and *risk seeking* individuals
- We assessed the methylation levels between the *patient* and *impatient* population groups

Variables Tested

NICOLA: Risk Preference

- For each of these choices below, which income do you choose?
- Income A, which will with certainty give you £1,500 per month for the rest of your life?
- Income B, which will give you a 50-50 chance of £3,000 and a 50-50 chance of £1,000 / £1,200 / £1,300 per month for the rest of your life?

NICOLA: Time Preference

- Would you rather have:
- £1,500 now?
- Or £1,506 / £1,512 / £1,518 / £1,524 / £1,536 / £1,548 / £1,596 a month from now?

Procedure

Step 1

NICOLA participant data and blood collection

Step 2

MethylationEPIC (Illumina):

Evaluation of >850,000 CpG sites

Step 3

Data quality control and analysis:

Partek Genomics Suite v7.0

Differential Methylation Analysis

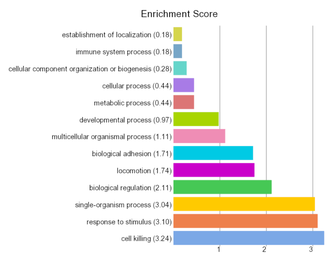
- ANOVA tests were carried out to determine CpG sites with a differential methylation status ($p<10^{-05}$):
  - Patient *vs* impatient population groups
  - Risk averse *vs* risk seeking population groups
- Gene ontology analysis was also conducted

Results: Time Preference

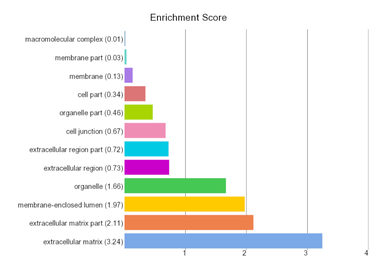
Top-ranked CpG sites: patient *vs* impatient

CpG Site	Gene	P Value	Fold-change
cg05355328	*ANKRD27*	$1.7x10^{-06}$	Increased in patient group
cg02406350	*NINJ2*	$2.3x10^{-06}$	Increased in patient group
cg02895509		$2.9x10^{-06}$	Decreased in patient group
cg19912619	*ABCB5*	$9.0x10^{-06}$	Increased in patient group

Gene Ontology



Biological Processes



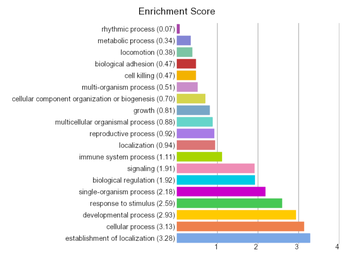
Cellular Components

Results: Risk Preference

Top-ranked CpG sites: risk averse *vs* risk seeking

CpG Site	Gene	P Value	Fold-change
cg05157098	*THAP2*	$6.4x10^{-09}$	Decreased in risk averse group
cg15810171	*YRDC*	$4.4x10^{-08}$	Decreased in risk averse group
cg20249566	*NWD1*	$6.4x10^{-08}$	Decreased in risk averse group
cg05308904		$8.9x10^{-08}$	Increased in risk averse group

Gene Ontology



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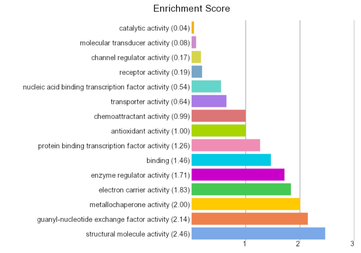

Molecular Function

Top-ranked CpG sites displaying evidence of a linear trend across the risk preference scale

CpG Site	Gene	Fold-change
cg13149459	*PPP1R12B*	Increased in risk averse group
cg00063654	*RFTN1*	Increased in risk averse group
cg15990008	*PPP1R12B*	Increased in risk averse group
cg13150977	*UBE2QP1*	Decreased in risk averse group

Conclusion

- DNA methylation may represent potential important biomarkers of accumulated, complex environmental determinants of these traits and their relationship to health behaviours
- Several striking results from this study support the need for further analysis of DNA methylation as an important link between measurable biomarkers, health outcomes and additional exploration of the functional significance of these particular genetic loci
- Data from longitudinal cohorts provide the opportunity to monitor the relationship between time and risk preference, health behaviours (such as diet physical activity and smoking) and health outcomes

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