

# Longitudinal methylation changes in *SGK1* are associated with blood glucose levels in healthy Norfolk Island females

Miles Benton, Heidi Sutherland, Larisa Haupt, Rod Lea and Lyn Griffiths

## The Norfolk Island Genetic Isolate

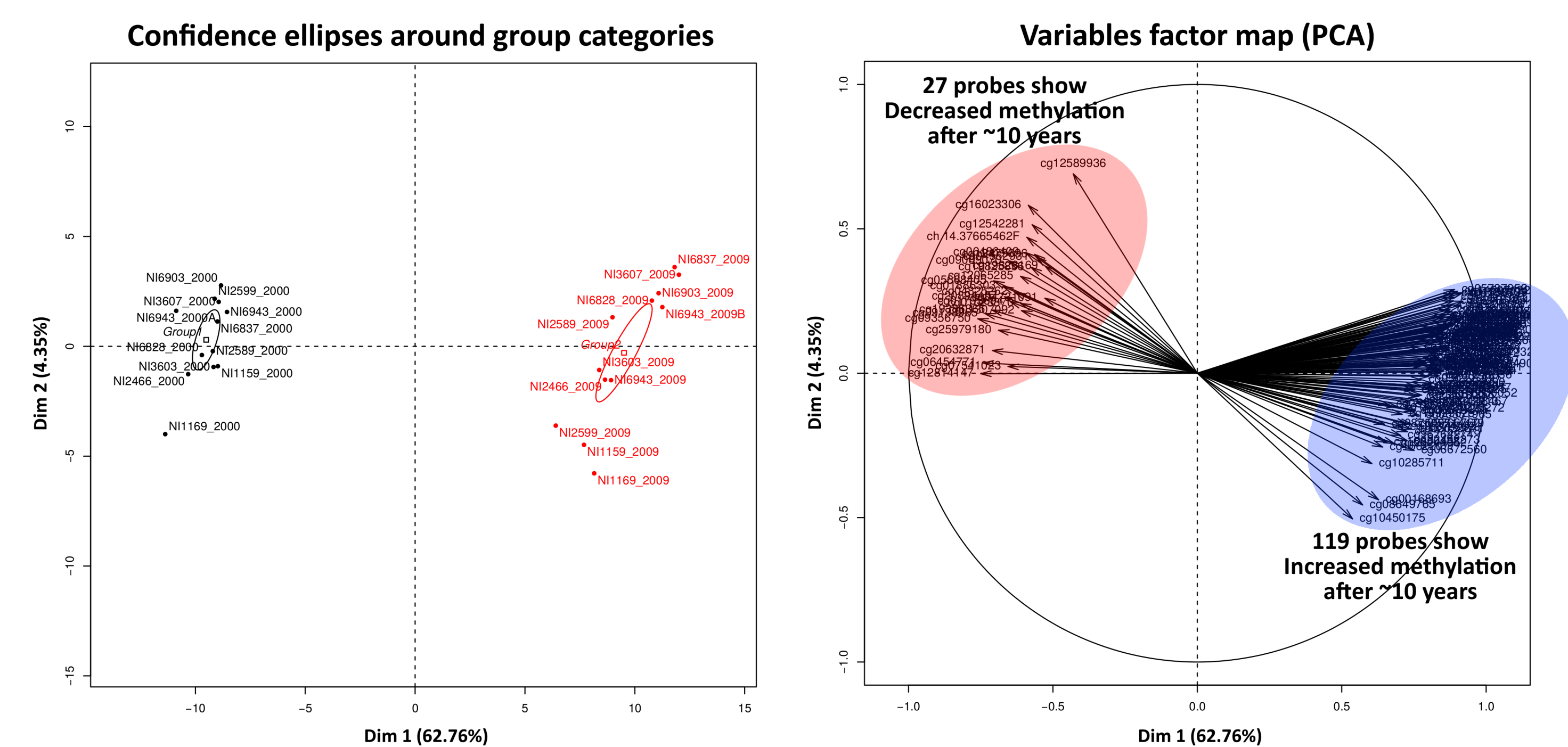


The current Norfolk Island population has arisen from a small number of founders with mixed Caucasian and Polynesian ancestry, descendants of a famous historical event - **The 'Mutiny on the Bounty'**.

- 12 samples, healthy Norfolk Island females
  - aged matched, never smoked, not on med's, healthy body metrics
- two time-points, year 2000 and 2009/2010 follow-up
- run across two **Illumina 450k** methylation chips (staggered design)

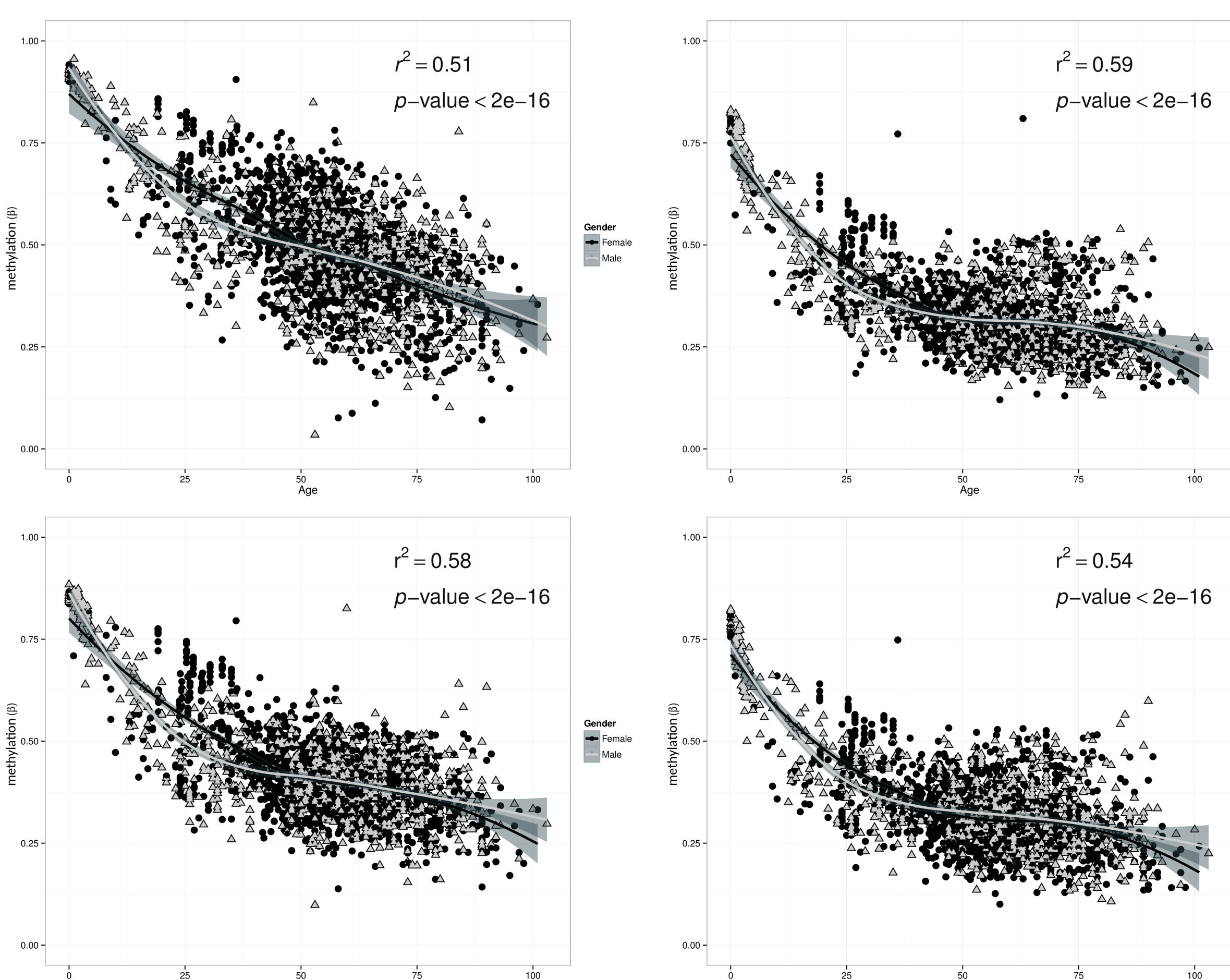
## Longitudinal Methylation Changes

- a binomial model with an elastic net was applied across all available CpGs
- PCA was used to visualise the separation of the individuals and variables (CpGs)



- identified **146** differentially methylated CpG sites
- 95%** located in genes, with the majority of these in 'traditional' control regions

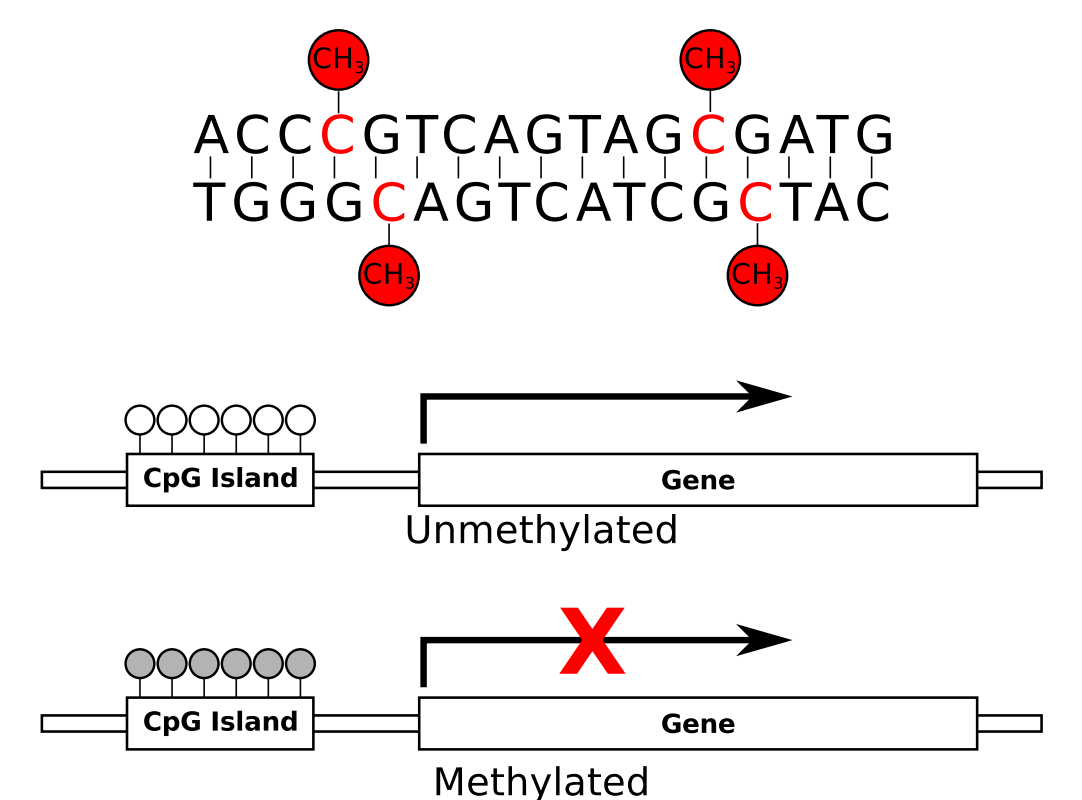
## An Example of the Ageing Methylome



- we further explored several of the age markers in ~2500 public samples
- striking methylation profiles exist across **100 years** of human life

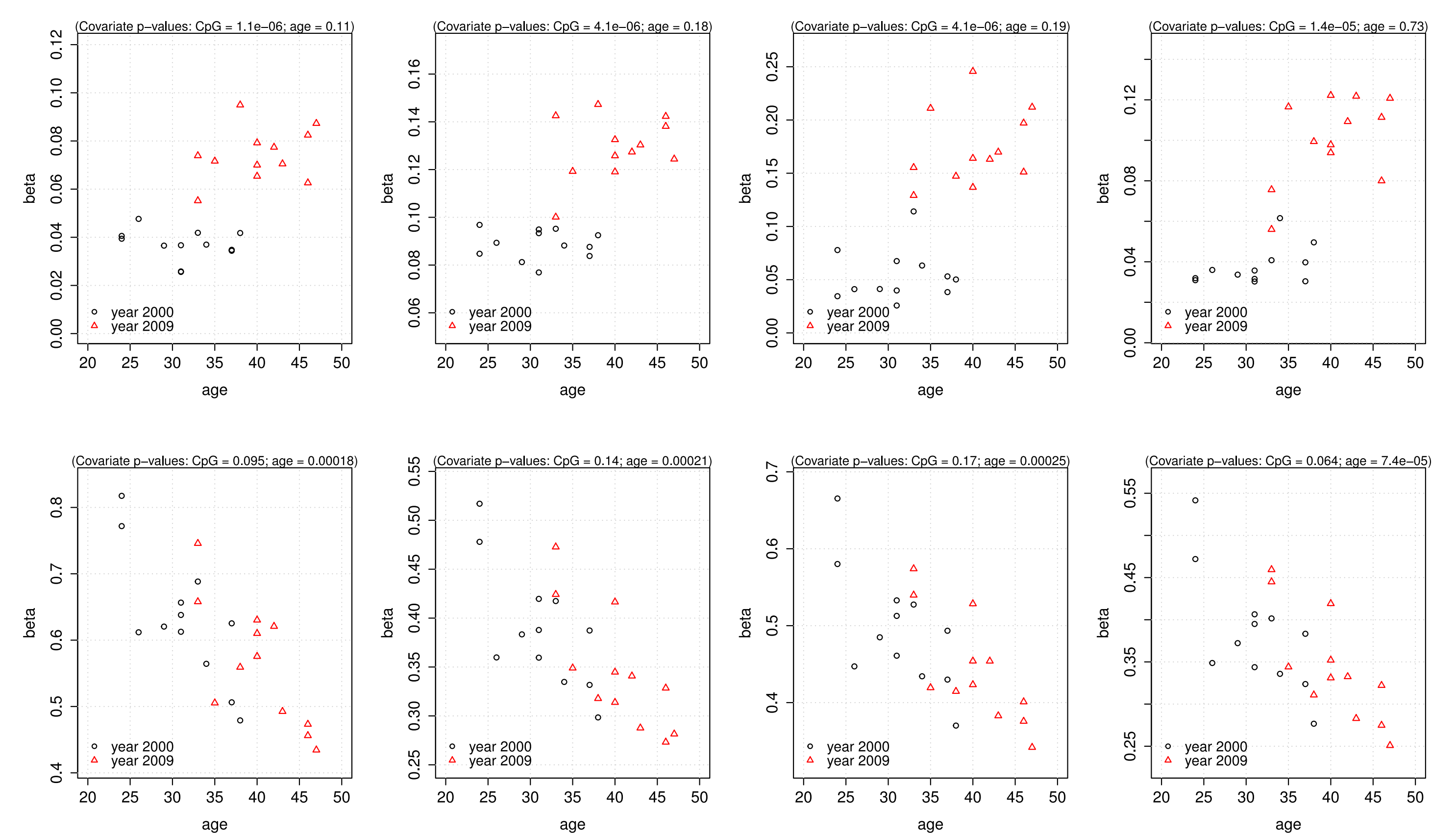
## Methylation: Genomic punctuation

"Woman without her man is nothing."  
 "Woman, without her man, is nothing."  
 "Woman! without her, man is nothing."



- methylation is heritable - imprinting (...other?)
- BUT** also **dynamic**: environment & other stimuli

## Time and Age are different entities



- separate series of distinct **age-markers** -> methylation changing in response to various environmental stimuli independent of the effects of the ageing process

## *SGK1* and Blood Glucose

- investigated associations between change in ( $\Delta$ ) methylation and clinical traits
- strong positive correlation was identified between  $\Delta$ glucose and  $\Delta$ CpG
  - ( $r=0.844$ ,  $p=0.001$ )
- interestingly *SGK1* is a kinase which is activated by insulin
  - may regulate insulin and GLUT4-dependent cellular glucose uptake

## Key findings to date...

- identified a strong longitudinal methylation signal in 12 healthy females
- report a distinct difference between longitudinal time and age
- significant longitudinal correlation between CpG sites in *SGK1* and **blood glucose**
  - may provide interesting insight into epigenetic regulation of complex diseases such as type-2 diabetes

**We demonstrate the utility and power of high-throughput DNA methylation arrays for fundamental biological and disease based research**

