

# DNA methylation as an additional tool in age estimation

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# Molecular biology-methods for age estimation

- Several methods have been proposed:
  - Telomere shortening
  - Mitochondrial mutations
  - Single joint T-cell receptor excision circle rearrangements



Variance is relatively large<sup>1</sup>

1. Bekaert et al. (2015) Improved age determination of blood and teeth samples using a selected set of DNA methylation markers, *Epigenetics*, 10:10, 922-930

# Epigenetics

- The genetic code of DNA is defined by the four bases A, C, G and T
- However, there are other regulatory mechanisms that define an organism

# DNA methylation

- Is a modification to DNA through the addition of a methyl group to the DNA strand itself, often the 5 carbon position of cytosine (usually when it's situated next to G, called CpG)
  - Called epigenetic because it does not affect the DNA sequence
  - Maintained through cell division and can be inherited

# DNA methylation

- An essential regulatory mechanism of several vital functions in humans, for example:
  - Embryogenesis
  - X-chromosome inactivation
  - Genetic imprinting (heritable)
  - Cell division
  - Gene regulation
- Less vital phenomena:
  - Aging
  - Cancer
  - Certain autoimmune diseases
  - Etc...

# DNA methylation and aging

- Approximately 1/3 of all CpG's in the genome are influenced by age
- Some sites of the DNA are methylated and some are de-methylated with increasing age
- Methylation is an active process performed by enzymes
- De-methylation can be done by enzymes or happen spontaneously
- Certain genes that change expression level with increasing age also change methylation level

# DNA methylation

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- Conserved through evolution

# How is methylation measured?

- Several methods exist
- The most used is Infinium<sup>®</sup> HumanMethylation450 BeadChip:
  - Analyzes more than 485 000 methylation sites from 1μl of e.g. blood
  - Approx 300 USD per sample



# DNA methylation and age estimation

- Some studies are prospective
- Some take data from databases
- Use different sample types (blood, saliva, teeth cells) and different markers
- Databases like GEO (NCBI) and TCGA (The Cancer Genome Atlas)

# DNA methylation studies (Illumina)

# Horvath et al. (2013)

- Developed a multi-tissue predictor of age
- Analyzed 7844 samples from 82 data sets in 51 different types of cells
- The analysis involves 353 probes (193 positively and 160 negatively correlated with age)
- Most tissues had comparable rates of methylation aging
- The model is logarithmic up to 20 years and linear after that

# Bekaert et al. (2015)

- Aimed to reduce the number of markers
- Analyzed blood (and teeth)
- Picked out 4 candidate genes that were reported to be relevant in the aging process
- Used a quadratic regression model

# Future work

- Optimize the prediction model for our age interval (e.g. 12-25 years)
- Identify and quantify the impact of unsystematic variables:
  - Ethnicity
  - Sex
  - Traumatization
  - «Socioeconomic factors»
- Build experience in using and improving the tool
- Expand the amount of data