Epigenetics—where the environment meets the genetics of disease: Interpreting high-throughput DNA Methylation data

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Epigenetics: An Overview

- **Epi-(GREEK:over,above) genetics**
  - heritable changes in gene expression/phenotype
  - functionally relevant changes, doesn’t modify underlying genomic sequence

- Several mechanisms:
  1. Histone modifications (Acetylation and Methylation)
  2. DNA Methylation
A brief overview of DNA Methylation

- 5’methylation of cytosine
- typically at CpG dinucleotide

Result is a reduction of gene expression (though there are exceptions)

- Methylation is heritable - imprinting
- **BUT** is also dynamic: response to environment
The Illumina 450K Human Methylation Chip

- **Illumina 450K Human Methylation Chip**
  - Genome Wide: has >450,000 probes (individual CpG sites)
  - only recently publications starting to emerge
  - analysis needs to catch up

- DNA is Bisulfite converted, fragmented and hybridised.
- Difference in intensity between meth/unmeth probes gives Beta.

**Beta Values**

\[ \beta = \frac{\text{meth}}{\text{meth} + \text{unmeth} + 100} \]

Values range between 0-1
- think of as percent methylation
Study Design is Crucial

Need to really think about study design:

- Same old story: Quality in equals Quality out
  - good bioinformatics will never make up for poor lab technique and/or poor study design

- Gender - sex specific methylation patterns

- Origin of sample (i.e. blood, tissue)
  - mixed cell populations

- Case/Control? Paired-samples? Numbers?
Example: Gender and Tissue specific markers

cg10422744  
NI_blood  
Esr_ab  
Esr_om  
gender  

cg03278611  
gender  

cg20256263  
tissue  

cg21983484  
gender  

cg06946770  
tissue  

cg13408286  
tissue  

cg25012947  
gender  

cg14083015  
tissue  

cg16379462  
tissue  

cg11962640  
tissue  

cg20485084  
tissue  

cg08059778  
gender  

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Investigating Methylation Profiles in Blood Cells

Publicly available data set (6 'healthy' males) - cell sorted

- cg01477015 : CD19 () CHR: 16 (28948319)
- cg01758575 : CD19 () CHR: 16 (28943288)
- cg03660502 : CD19 () CHR: 16 (28948092)
- cg05433111 : CD19 () CHR: 16 (28943232)
- cg05981394 : CD19 () CHR: 16 (28942152)
- cg06323049 : CD19 () CHR: 16 (28943094)
- cg07322144 : CD19 () CHR: 16 (28948179)
- cg07597976 : CD19 () CHR: 16 (28943019)
- cg09989938 : CD19 () CHR: 16 (28944403)
- cg14102807 : CD19 () CHR: 16 (28943677)
- cg2490063 : CD19 () CHR: 16 (28948266)
- cg27565966 : CD19 () CHR: 16 (28943198)
'Global' Methylation Profiles (MARMAL-AID)

- TSS1500
- TSS200
- 5'UTR
- 1stExon
- Body
- 3'UTR
- Intergenic

average beta

cell/tissue types
- Prostate
- Breast
- Tongue
- Eye
- Heart
- Stomach
- Bone
- Liver
- Kidney
- Bladder
- Lung
- Blood
- Skin
- Brain
- Adipose
- Ab_pre
- Ab_post
- Om_pre
- Om_post

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