

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

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Epigenetics: An Overview

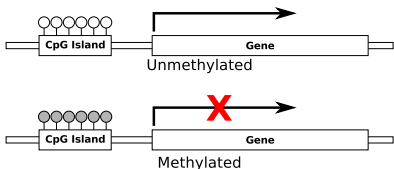
- Epi-(GREEK:over,above) genetics
 - heritable changes in gene expression/phenotype
 - functionally relevant changes, doesn't modify underlying genomic sequence
- Several mechanisms:
 - ① Histone modifications (Acetylation and Methylation)
 - ② **DNA Methylation**

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

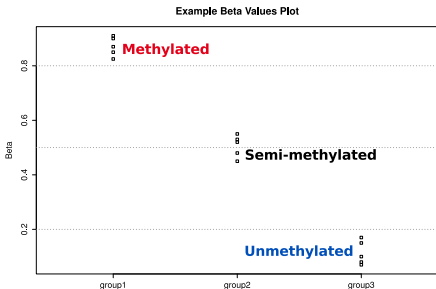
- Illumina 450K Human Methylation Chip
 - Genome Wide: has >450,000 probes (individual CpG sites)
 - only recently publications starting to emerge
 - analysis needs to catch up
- DNA is Bisulfite converted, fragmented and hybridised.
- Difference in intensity between meth/unmeth probes gives Beta.

Beta Values

$$\beta = \frac{\text{meth}}{\text{meth} + \text{unmeth} + 100}$$

Values range between 0-1

- think of as percent methylation

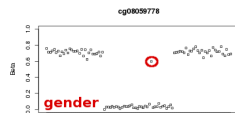
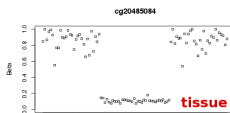
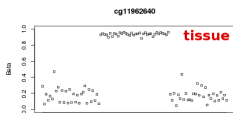
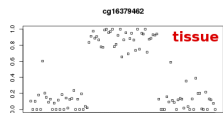
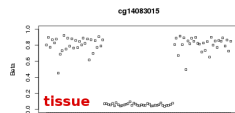
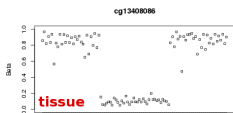
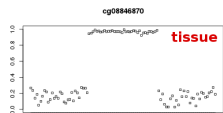
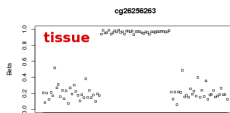
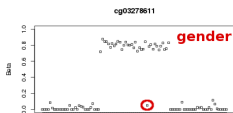
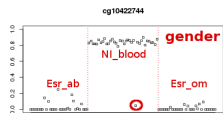


Study Design is Crucial

Need to really think about study design:

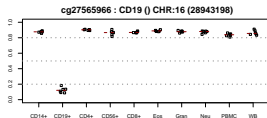
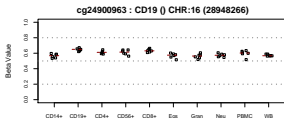
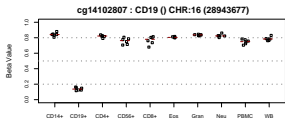
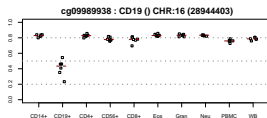
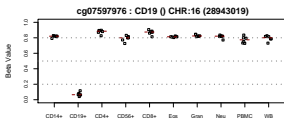
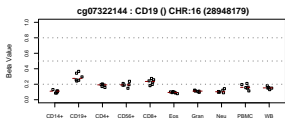
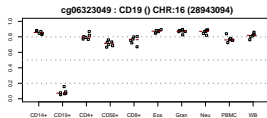
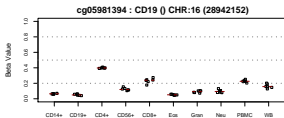
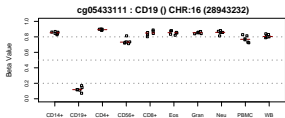
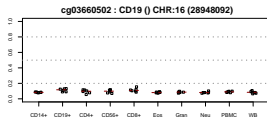
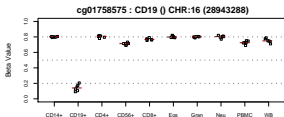
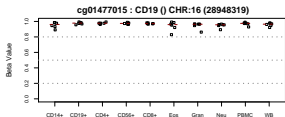
- Same old story: Quality in equals Quality out
 - good bioinformatics will never make up for poor lab technique and/or poor study design
- Gender - sex specific methylation patterns
- Origin of sample (i.e. blood, tissue)
 - mixed cell populations
- Case/Control? Paired-samples? Numbers?

Example: Gender and Tissue specific markers

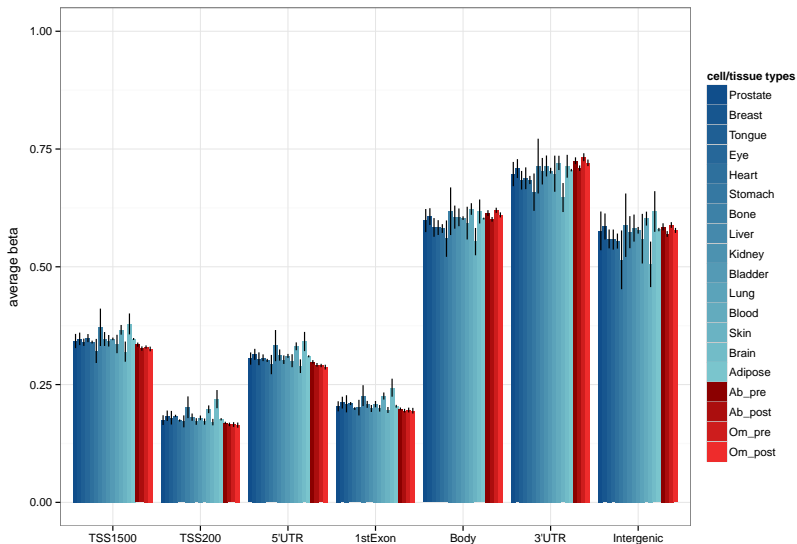


Investigating Methylation Profiles in Blood Cells

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



'Global' Methylation Profiles (MARMAL-AID)



Acknowledgements

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