

# Epigenomics

Objective: To give a presentation of about 60 minutes at the end of the week covering the key aspects of the epigenetics/epigenomics.

Epigenetics is the structural and chemical modification DNA in a cell that is inheritable from ancestor cell to daughter cell and thus provides a heritable way of tagging DNA (in particular DNA methylation and histone modification) that serves a variety of purposes for the organism. Epigenomics is epigenetics on a genomic scale. Methylation is more stable, so changes in methylation patterns are typically longer lasting than histone modifications which might only last for the duration of the cell life. Methylated DNA (mainly methylated cytosines) and histone modifications can be detected using chromatin immunoprecipitation techniques. There are specific antibodies against 5-methyl cytosine which can be used to immunoprecipitate methylated DNA fragments and similarly there are specific antibodies against various modified histones which can be used to immunoprecipitate the modified histone proteins. These fragments can then be washed, amplified and hybridised to microarrays. Bisulphite treated DNA can also be used to detect methylated C's since the treatment converts unmethylated C's to T's. Bisulphite DNA can be hybridised to an array to distinguish methylated positions. To reduce the dimension and the number of arrays required (for both ChIP-on-chip and Bisulphite treatment methods), the arrays used usually contain probes from gene promoter regions. Epigenetic processes are widespread throughout the genome. Epigenetic features are primarily inherited but they are subject to modification over time; either due to environmental sensitivity or stochasticity associated with inaccurate copying mechanisms. The effects of an epigenetic change/mutation can be passed onto daughter cells (e.g. cancer tumour growth) or be temporary and last only a single cell cycle. For example, the copying mechanisms associated with DNA methylation for example are only 96% accurate such that one error is expected every 25 methylated sites. Since the epigenome of an individual is dynamic over time, it is suggested that it could be responsible for incomplete penetrance of genetic disease. For example studies show that identical twins can exhibit vast differences at an epigenomic level and hence could be underlying discordant phenotype.

## The Big Questions Are:

- How does epigenetic mechanism arise and evolve?
- What are the major classes mechanisms?
- How are these mechanisms distributed phylogenetically?
- What is their distribution along the chromosomes on humans?
- What are the mutation rates in the different types
- When was epigenetic phenomena first discovered?

## Possible Contents of Presentation

History of the research of epigenetics

Experimental approaches to detection of DNA structural and chemical modification at a genomic scale

Major classes of epigenetic phenomena

The mechanisms of epigenetics and its control

The conservation and evolution of epigenetic phenomena over evolutionary time scales

## Starting points

<http://en.wikipedia.org/wiki/Epigenetics>

<http://www.epigenome.org/index.php?page=project>

<http://www.nature.com/omics/subjects/epigenomics/2009.html>

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Schones DE, Zhao K. Genome-wide approaches to studying chromatin modifications. *Nat Rev Genet.* 2008 Mar;9(3):179-91.

Wood & Oakey (2006) Genomic Imprinting in Mammals: Emerging Themes and Established Theories *PLoS Genetics* 2.1.147

Dodd et al. (2007) Theoretical Analysis of Epigenetic Cell Memory by Nucleosome Modification *Cell* 129, 813-822

Weber et al (2007) Distribution, silencing potential and evolutionary impact of promoter DNA methylation in the human genome *Natu.Genet* 39.4 .457-

Gal-Yam et al. (2008) Cancer Epigenetics: Modifications, Screening, and Therapy *Annual Review Medicine* 59:267-80

Rando and Chang (2009) Genome-Wide Views of Chromatin Structure *Annu. Rev. Biochem* 78:245-71

Ptak and Petronis (2008) Epigenetics and Complex Disease: From Etiology to New Therapeutics *Annu. Rev. Pharmacol. Toxicol.* 48:257-76