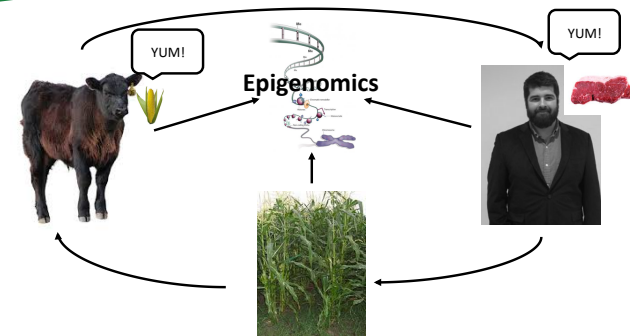


Basics and Prospects in Epigenetics

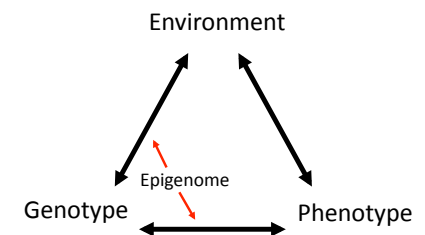
Beef Cattle → Plant Biologist?



Outline

1. Epigenetics vs Epigenomics
2. Methods of Analysis
3. Potential Applications
4. Conclusions

Epigenetics and Epigenomics

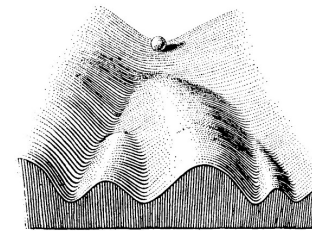


C. H. Waddington

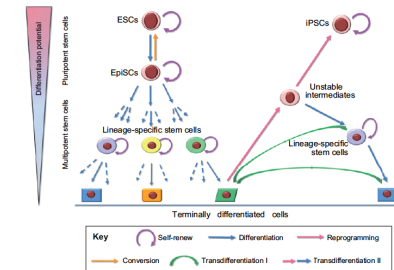
- Developmental Biologist
- Interested in **epigenesis**: Development of an organism from an undifferentiated state
- 1942: coined the term **Epigenetics** and concept of **Epigenetic Landscape** to describe how cells differentiated



The Epigenetic Landscape



Holliday, 1942



Zhang et al, 2012

Robin Holliday

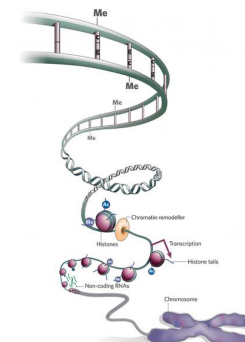
- Molecular Biologist
- Strand exchange during meiosis – Holliday Junction
- 1975 proposed DNA methylation as mechanism for regulation gene expression
- 1994 proposed two complimentary definitions of **Epigenetics**
 - “study of the changes in gene expression, which occur in organisms with differentiated cells, and the mitotic inheritance of given patterns of gene expression”
 - “nuclear inheritance, which is not based on differences in DNA sequence”



The Epigenome

Factors that interact with the genome, defining regions of heterochromatin and euchromatin

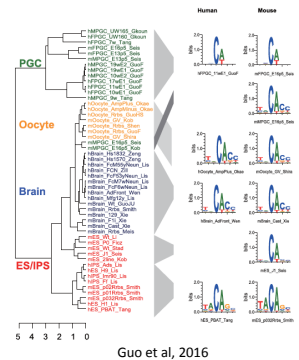
- DNA methylation
 - Hydroxymethylation
- Histone variants
- Histone modifications
- Small RNAs



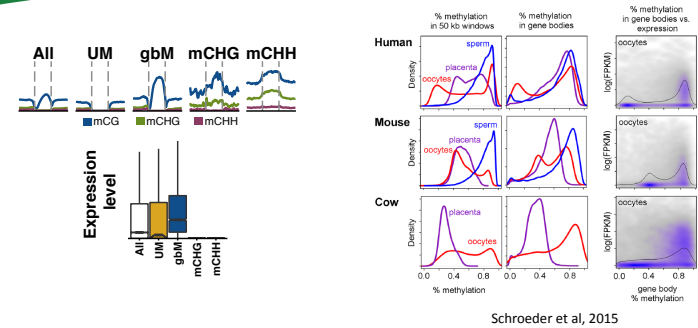
Nature **454**, 711-715 (7 August 2008)

Context Matters

- Methylation has different sequence contexts
- Plants
 - CG
 - CHG (H = A, T, or C)
 - CHH
- Animals
 - CG
 - CH

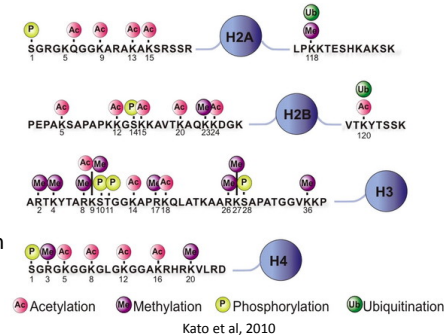


Context Matters



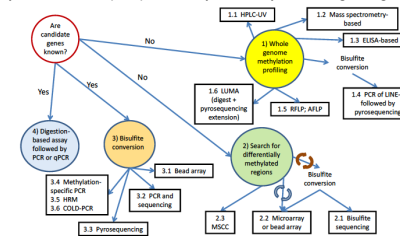
Histone Variants and Modifications

- “Histone Code”
- Different variants and modifications mark different domains of chromatin
- Associations with changes in gene expression



Methods of Analysis: DNA Methylation

Kurdyukov and Bullock (2016) DNA Methylation Analysis: Choosing the Right Method



Bisulfite Treatment

Unmethylated DNA: 5'-ACCGTCGACGT-3'

Methylated DNA: 5'-A⁺CGT⁺CGA⁺CGT-3'

- PCR
- Sanger Sequencing
- Arrays

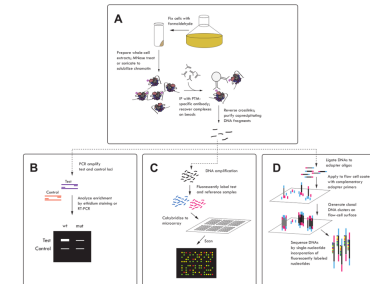


pacbio.com

nanoporetech.com

Methods of analysis: Histones

- Nucleosome occupancy
 - DNase-seq
 - ATAC-seq
 - MNase-seq
 - FAIRE-seq
- Chromatin Immunoprecipitation
 - Requires an antibody



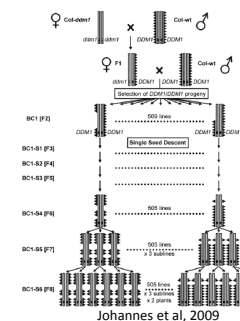
Applications of Epigenomics

- Selection and Breeding
- Predicting Performance
- Creating Epigenomic Variation
 - Environmental Manipulation
 - Epigenome Engineering and Manipulation



<https://www.citelighter.com/>

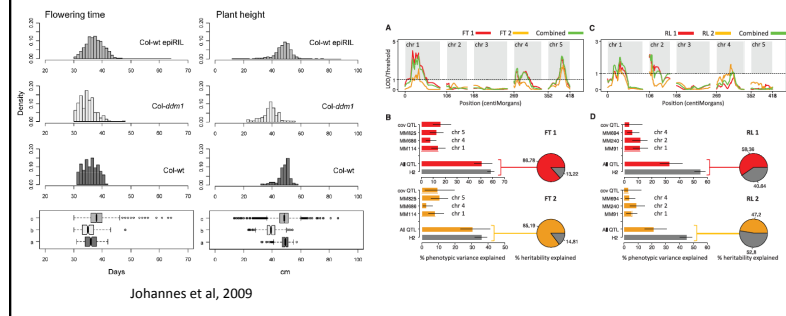
Selection and Breeding



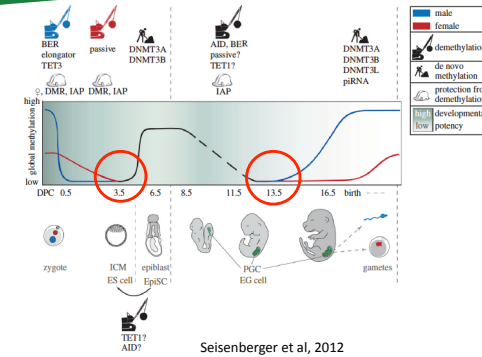
Roux et al, 2011

Johannes et al, 2009

Mapping Epigenetic QTL

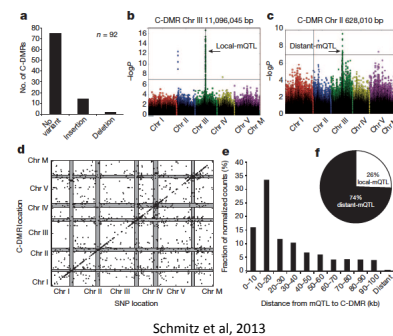


Mammals Reset the Epigenome

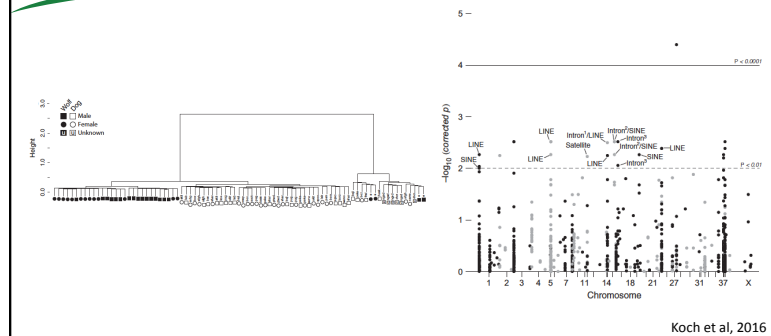


Genetic and Epigenomic Variation

- methyl-QTL (mQTL)
- Association of DNA methylation with genetic variation
- ~35% C-DMRs in Arabidopsis associate with an mQTL
- Likely an underestimate

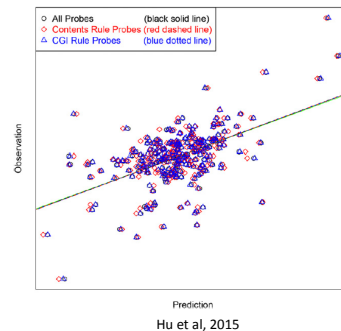


Dog Domestication Epigenomics



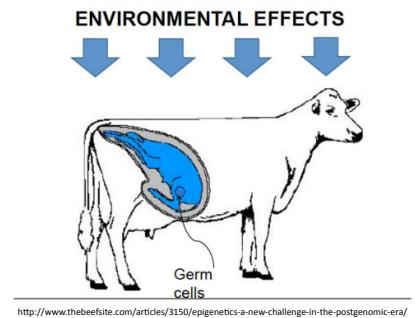
Predicting Performance

- Can epigenomic marks be used to predict traits?
- Predicting plant height using DNA methylation
 - epiRIL data
 - Predictive correlation: 0.532
 - Concluded epigenetic variation accounted for 65% of phenotypic variance

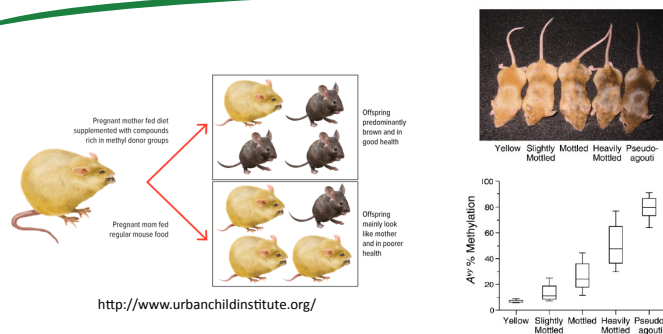


Environmental Manipulation

- The environment can affect the epigenome
- Can this be utilized to produce desirable outcomes?
- *In utero* effects?
 - Maternal imprinting
- Paternal effects (imprinting)?
 - Little evidence

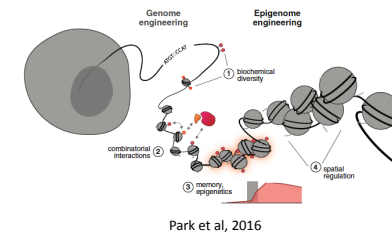


Agouti Gene, Diet, and Methylation



Epigenome Engineering and Manipulation

- How can we alter epigenomes and create variation artificially?
- Chemical Manipulation
- Genome-wide Engineering
- Targeted Epigenome Engineering



Genome-wide Engineering

Conclusions

- **Epigenetics:** “nuclear inheritance, which is not based on differences in DNA sequence”
- Variety of methods for analysis
 - Sequencing approaches have highest resolution, but are expensive
- Applications of Epigenetics and Epigenomics
 - Resetting of epigenome and cost of sequencing limit possibilities
- Lots of opportunity in Beef Cattle Epigenomics