

Epigenetics of methylation

BIOL 426/626
Approaches to Molecular Biology



Class 20: Epigenetics



- **Learning Goal**
 - To understand the dynamics of DNA modification during development and the methods used to analyze the modification state genome wide with single nucleotide accuracy
- **Learning Objectives**
 - Explain the role of CpG island methylation in regulating gene expression globally in the genome
 - Describe how bisulfite sequencing is used to identify sites of DNA methylation
 - Summarize how patterns of methylation can vary based on sex, developmental stage or tissue type
 - Discuss the role of DNA methylation in suppressing transposition by retroelements in the genome
 - Explain how DNA methylation is used for the epigenetic control system called imprinting
- **Reading assignment:**
 - Smith et al. A unique regulatory phase of DNA methylation in the early mammalian embryo. *Nature*. 2012 484:339-344.

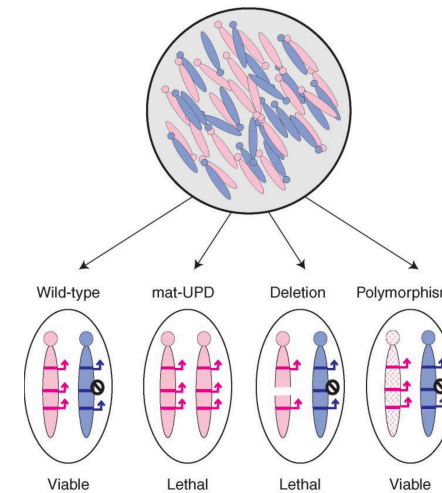
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Imprinting associated lethality



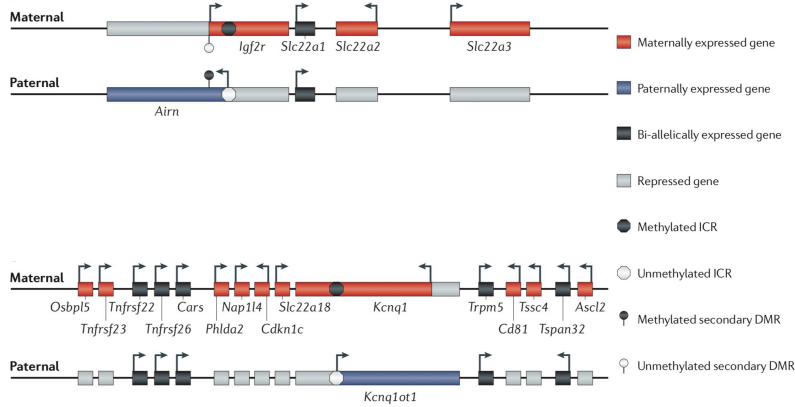
Diploid chromosome set
Wild-type embryo



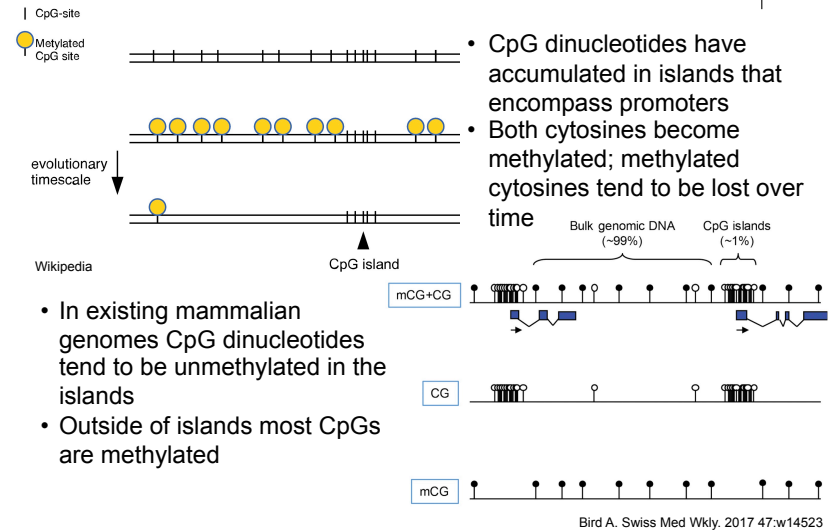
Barlow & Bartolomei CSH Perspect Biol. 2014 1:6 BIOL 426/626: Approaches to Molecular Biology

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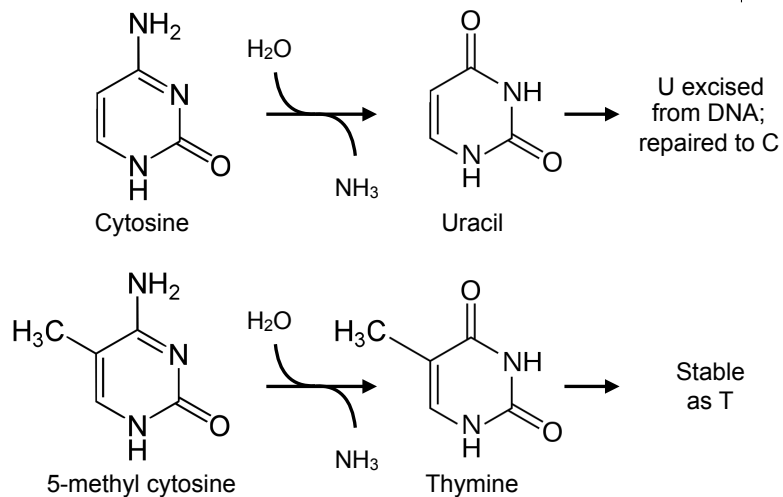
Examples of maternal imprinting



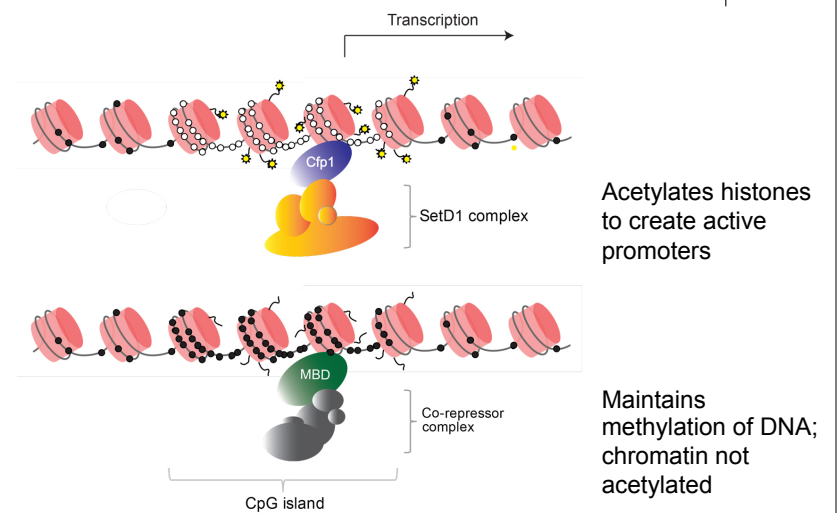
CpG "Islands"



5-methylcytosine tends to be lost

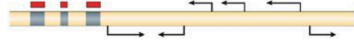


Methylation & expressed vs silent chromatin

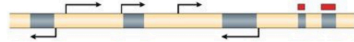


Different modes of methylation

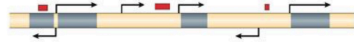
a Mosaic DNA methylation (fungi, for example, *Neurospora crassa*)



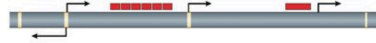
b Mosaic DNA methylation (plants, for example, *Arabidopsis thaliana*)



c Mosaic DNA methylation (animals, for example, *Ciona intestinalis*)



d Global DNA methylation (animals, for example, *Homo sapiens*)



e Global DNA methylation (plants, for example, *Zea mays*)



Gray: methylated
Yellow: unmethylated

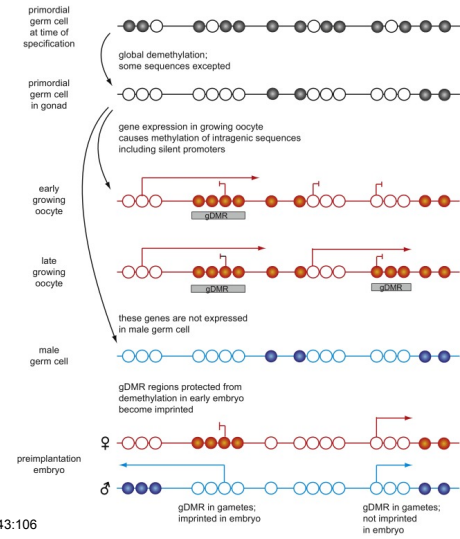
Suzuki & Bird Nat Rev Genet. 2008 9:46

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Patterns of changes in modification during gametogenesis and early development

Filled = C
Empty = 5meC

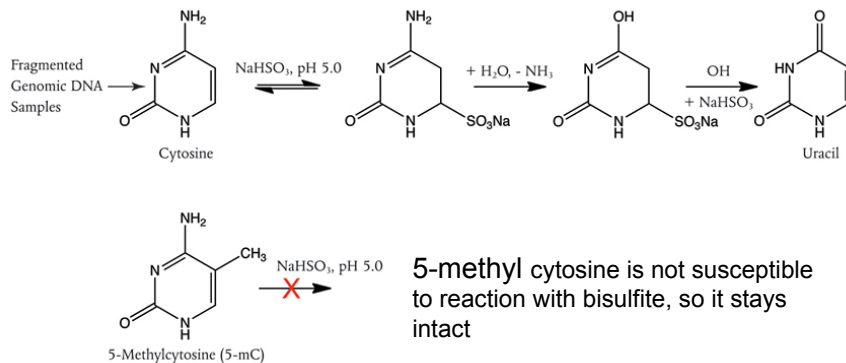


Clark & Vieux Seminars in Cell Dev Biol 2015 43:106

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Bisulfite sequencing

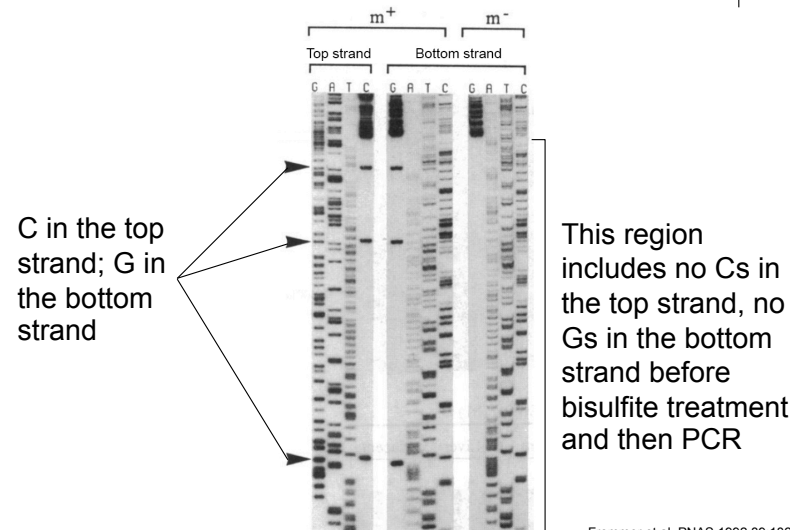


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Sequences of PCR products after bisulfate treatment

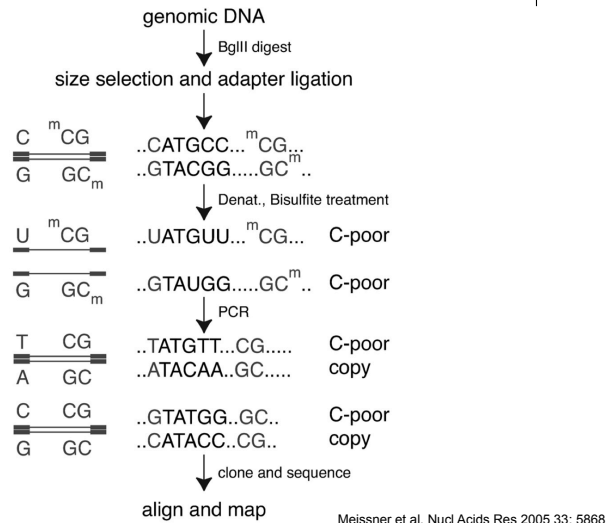


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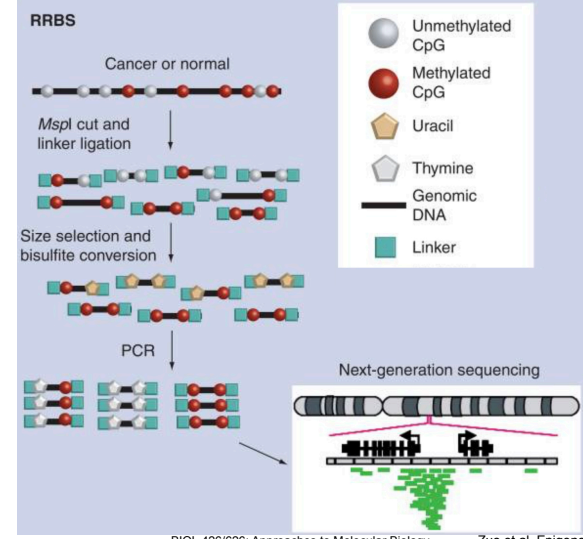
Frommer et al. PNAS 1992 89:1827

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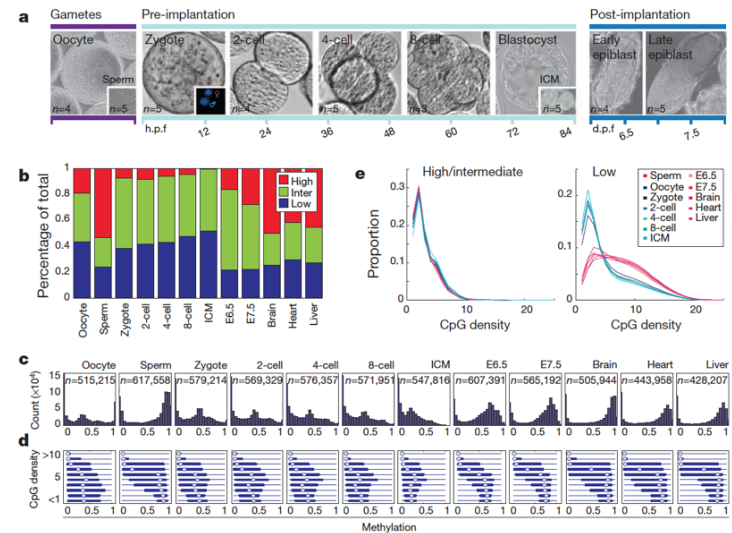
Reduced representation bisulfite sequencing



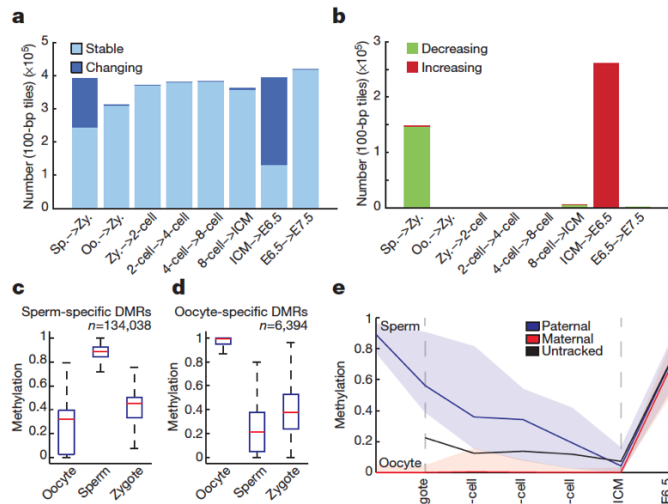
Reduced representation bisulfite sequencing



Smith et al., Figure 1



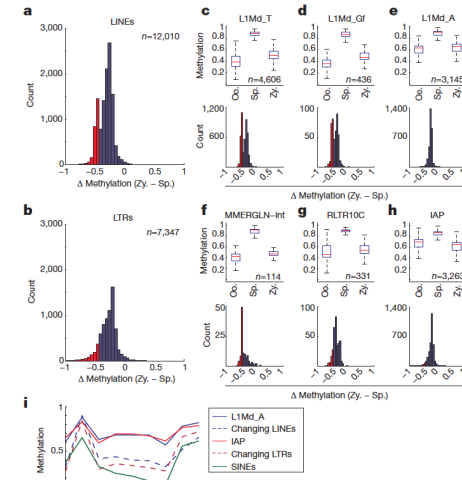
Smith et al., Figure 2



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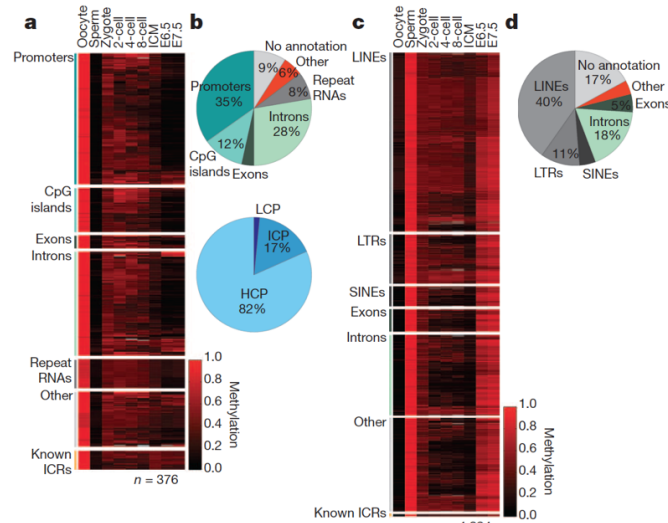
Smith et al., Figure 3



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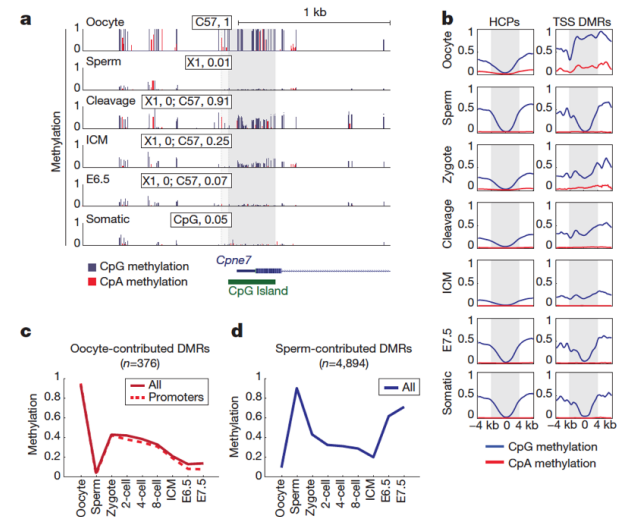
Smith et al., Figure 4



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Smith et al., Figure 5



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Reading for next time:



- Dale et al. *From Genes to Genomes*, Chapter 11
- Rydning et al. Conditional transgenic technologies. *J. Endocrinol.* 2001. 171, 1-14