

# Epigenetics - part 1

---



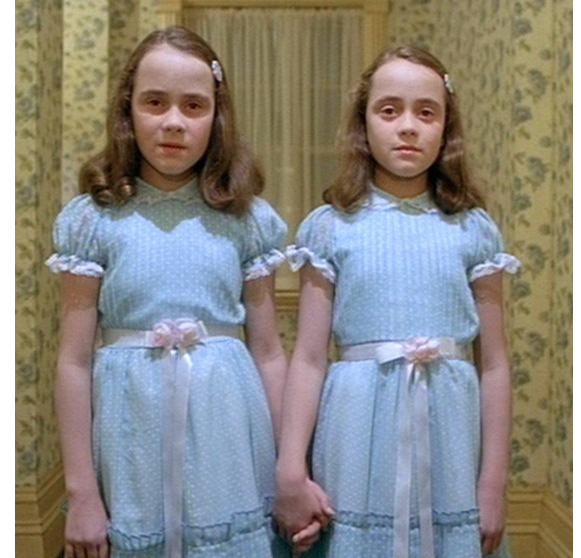
# Nurture or nature?

---

Given the same sequence of DNA, should we expect the same phenotypic outcome?

Or put another way, can the results of experience be heritable (excepting mutagen exposure)?

Epigenetics - heritable changes of DNA, not involving sequence changes, that regulate gene expression



# Levels of epigenetic regulation

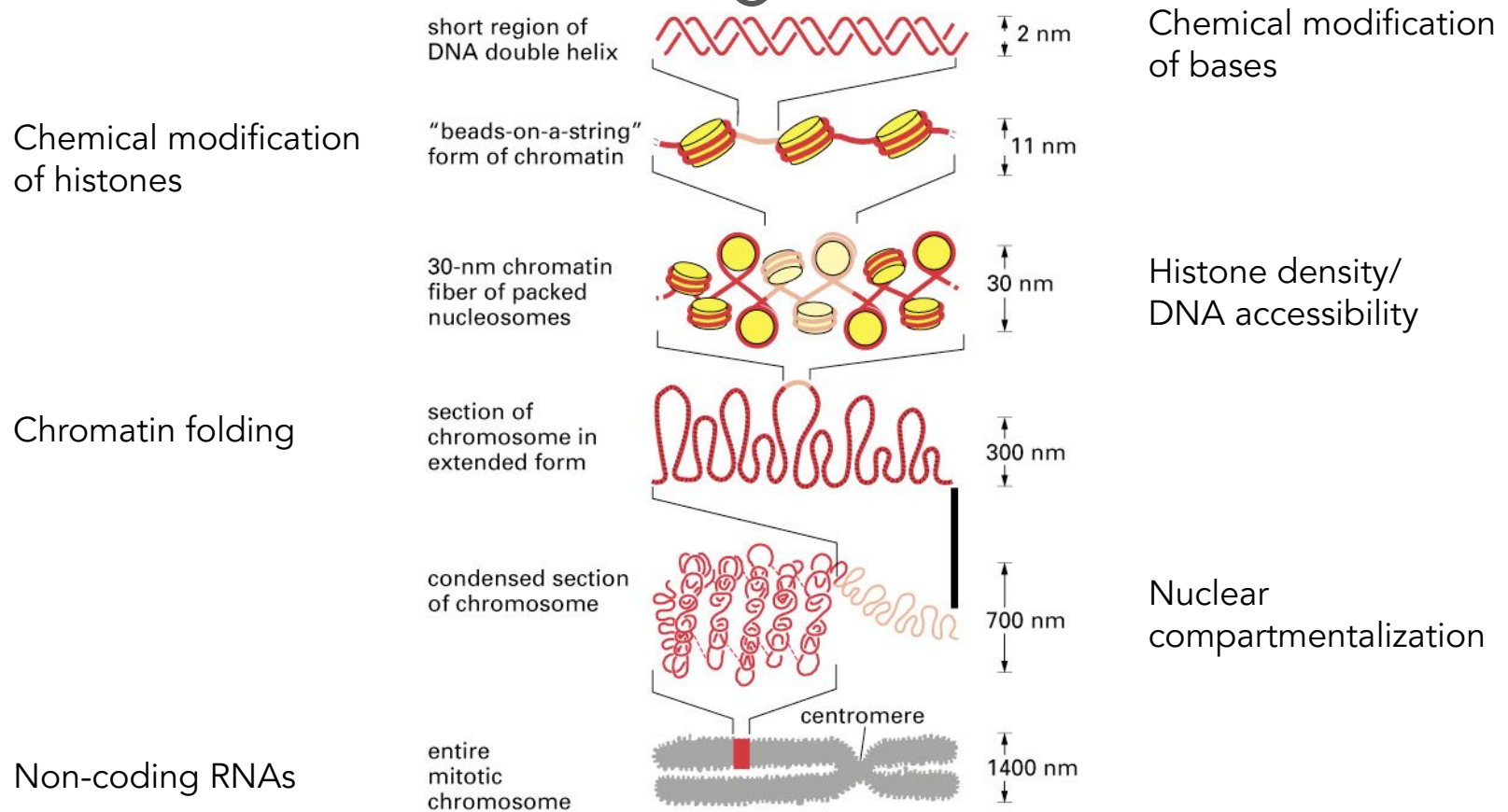


Figure 4-55. Molecular Biology of the Cell, 4th Edition.

# Levels of epigenetic regulation

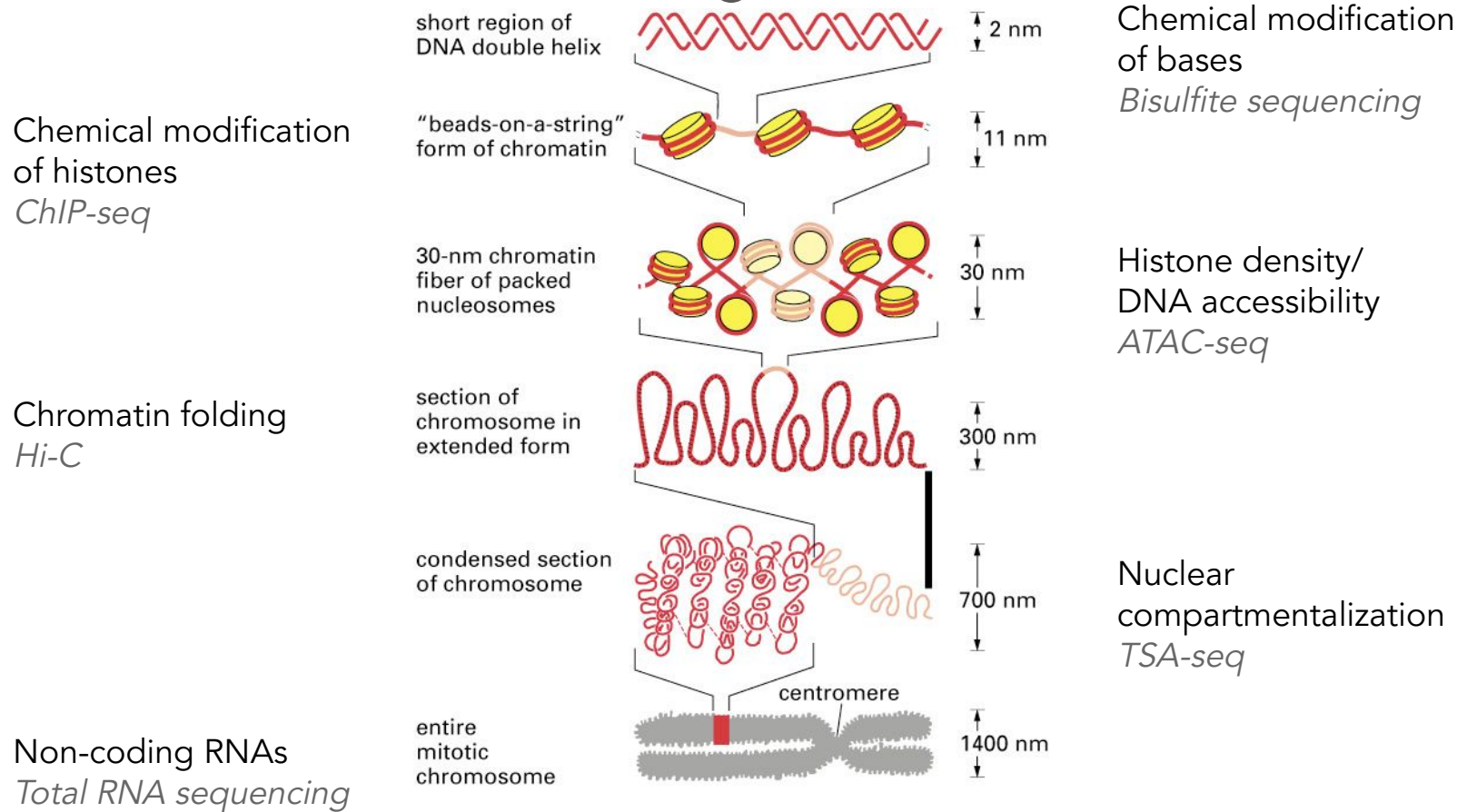


Figure 4-55. Molecular Biology of the Cell, 4th Edition.

# The epigenetic players

---

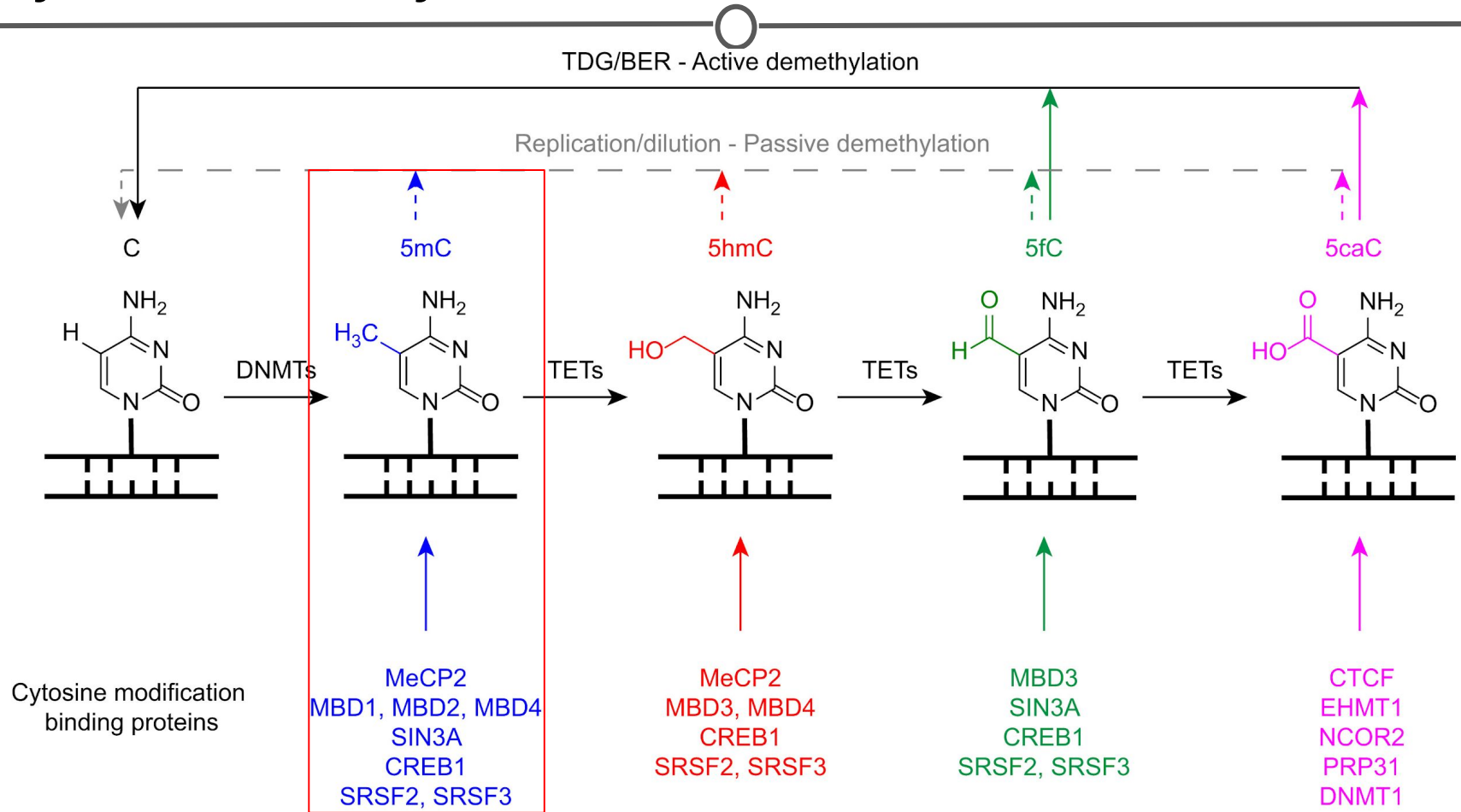
Out of ~25,000 coding genes, roughly 1000 are involved in epigenetic control

- DNA methylation:
  - DNA methylases/demethylases
- Histone modifications:
  - methylases, demethylases, acylases, ubiquitinases, readers, ...
- Nucleosome positioning:
  - Pioneer factors (Oct4, Sox2, Pou2, ...)
- Chromatin folding:
  - CTCF, cohesin, YY1, topoisomerase, ...
- ncRNAs:
  - Xist, piwiRNAs, lncRNAs, siRNAs, ...

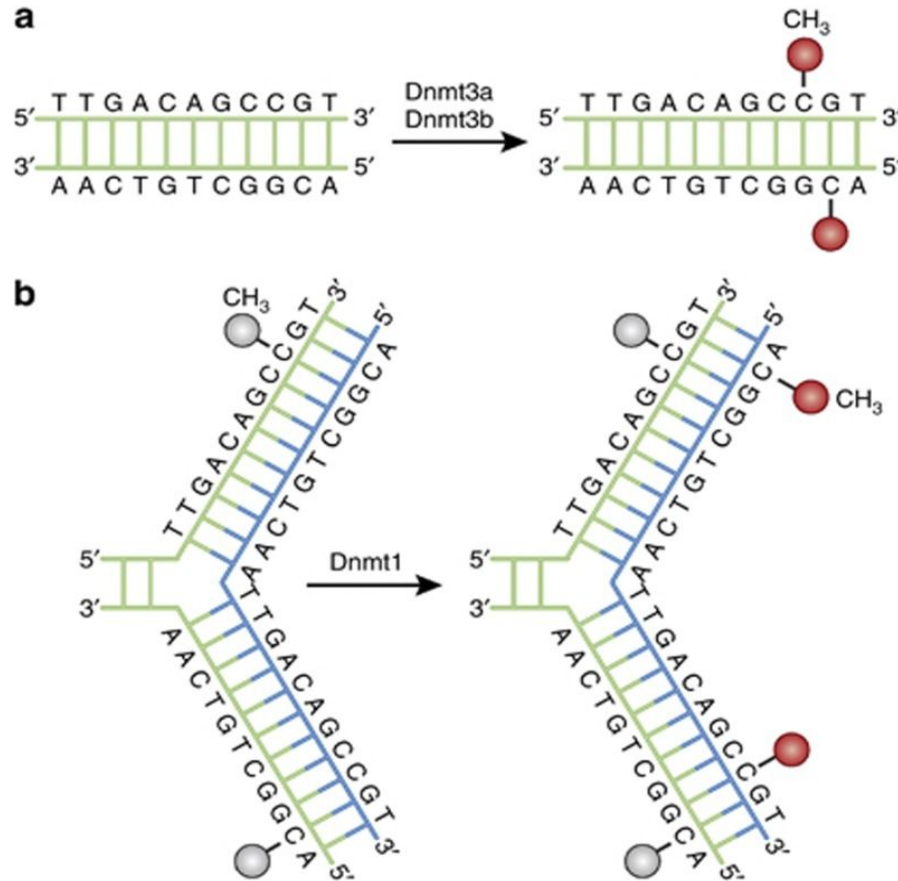
# DNA methylation



# Cytosine methylation



# Maintenance of 5mC through replication

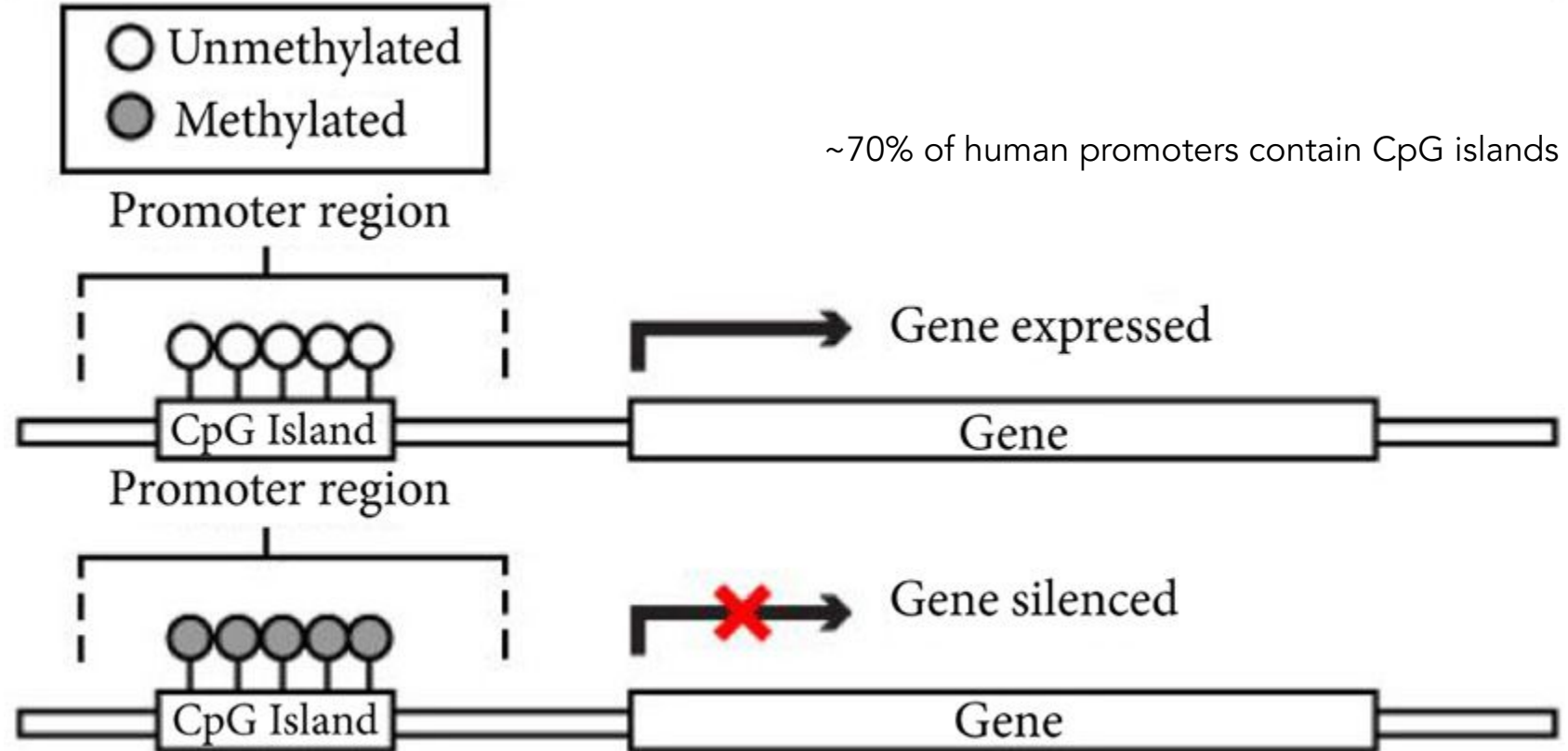




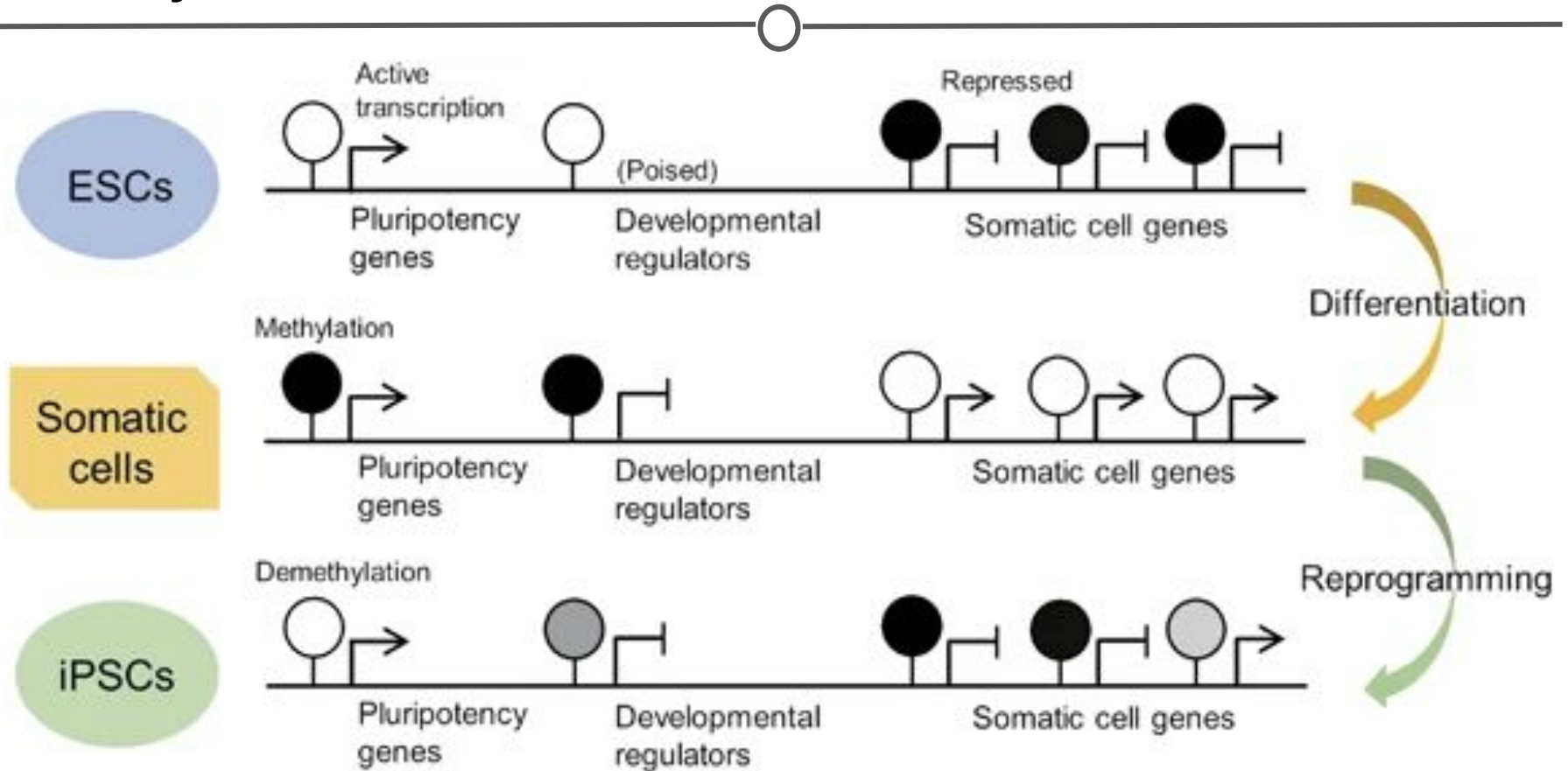
# Effects of DNA methylation



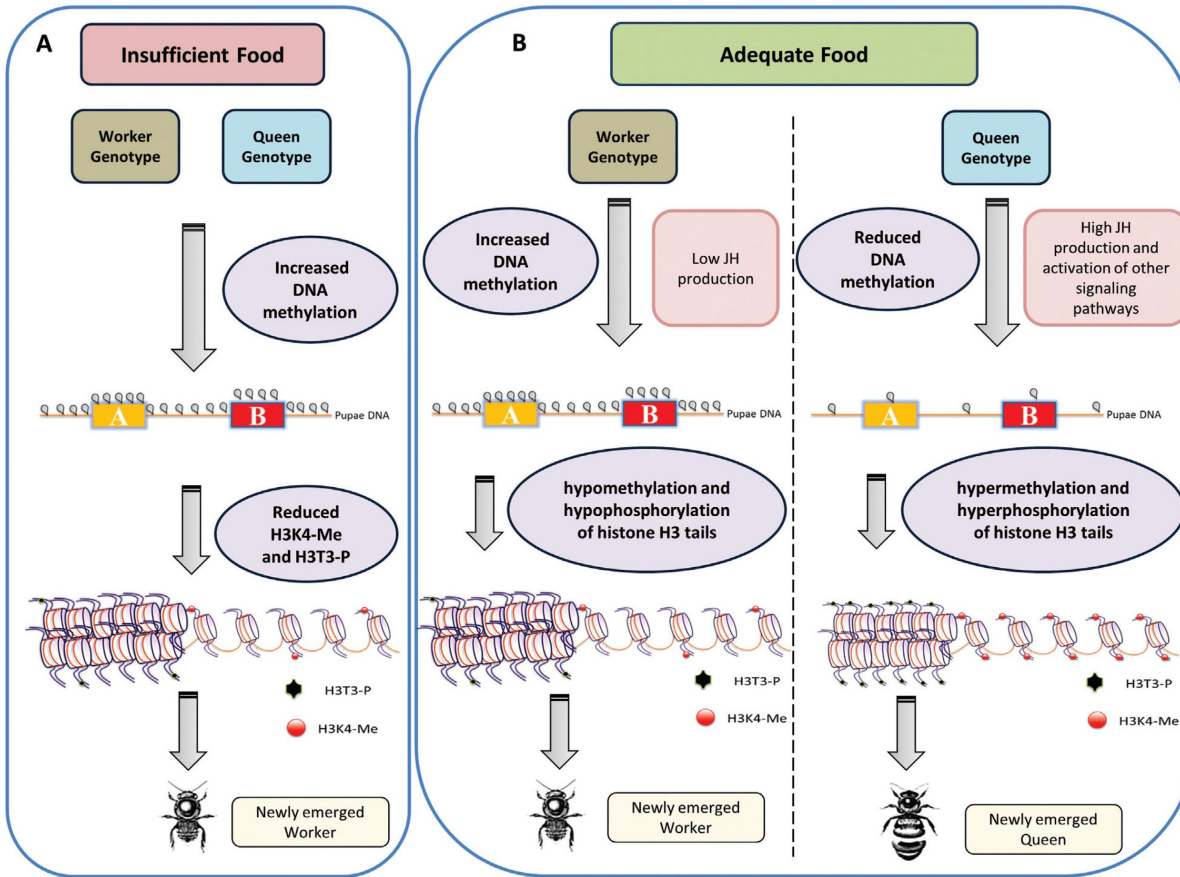
# CpG islands and gene regulation



# Methylation reinforces differentiation



# Environmental cues and methylation



Cardoso-Júnior Carlos A.M., Fujimura Patrícia Tieme, Santos-Júnior Célio Dias, Borges Naiara Araújo, Ueira-Vieira Carlos, Hartfelder Klaus et al .  
 Epigenetic modifications and their relation to caste and sex determination and adult division of labor in the stingless bee *Melipona scutellaris*. *Genet. Mol. Biol.* 2017 Mar; 40(1): 61-68.

# Suppression of transposable elements (TEs)

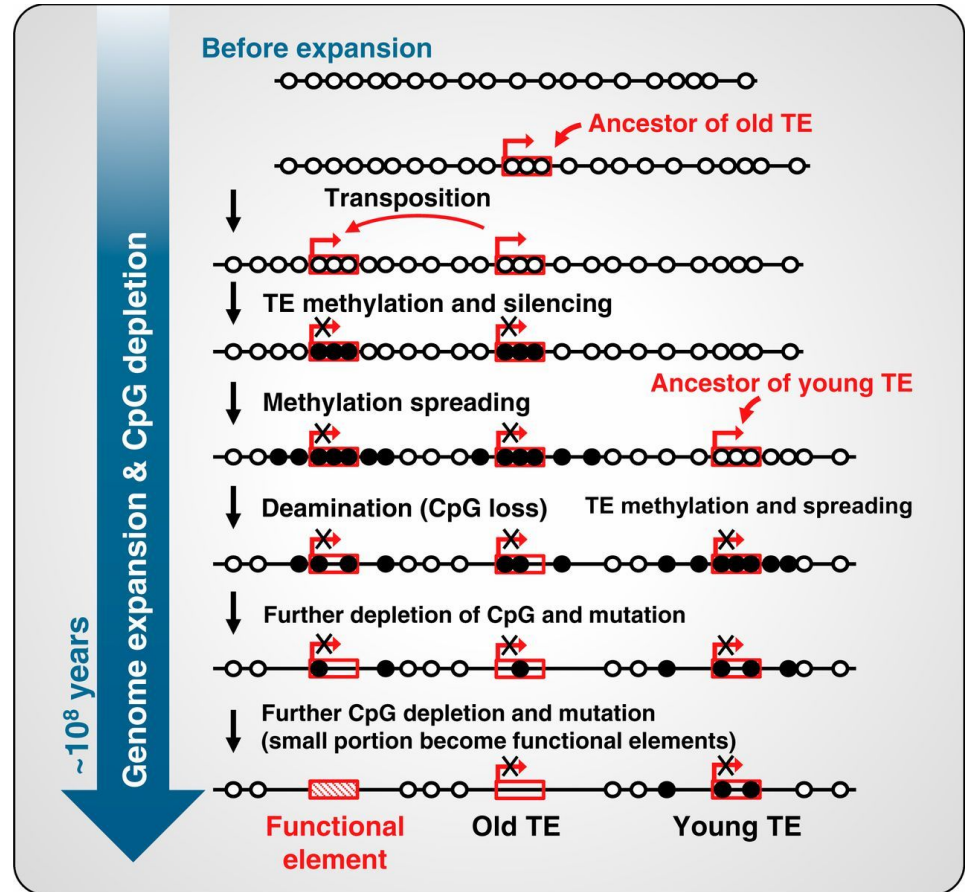
TEs are mobile repetitive sequences that can replicate and integrate into the genome

Two classes:

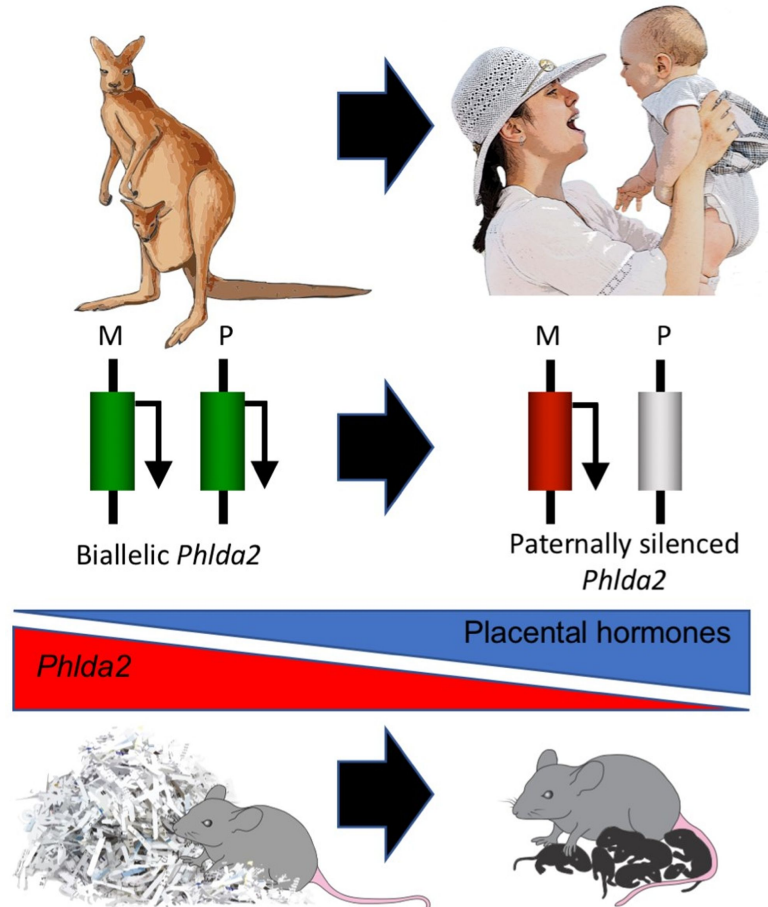
Class 1 - RNA intermediate

Class 2 - DNA intermediate

Make up ~45% of the human genome



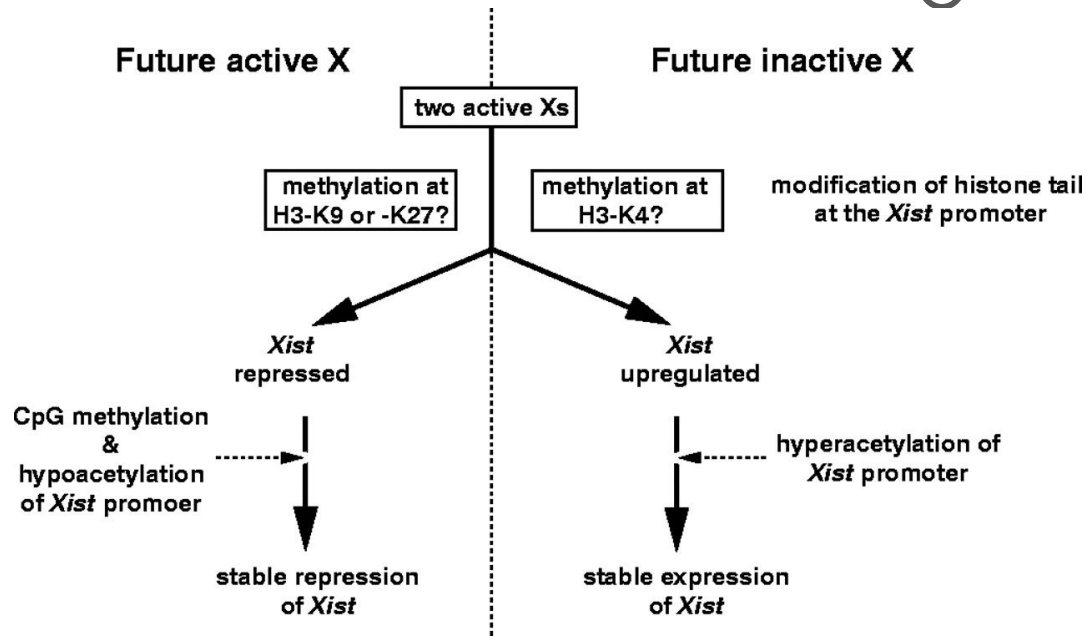
# Genetic imprinting



Creeth HDJ, McNamara GI, Tunster SJ, Boque-Sastre R, Allen B, Sumption L, Eddy JB, Isles AR, John RM. Maternal care boosted by paternal imprinting in mammals. PLoS Biol. 2018 Jul 31;16(7):e2006599.

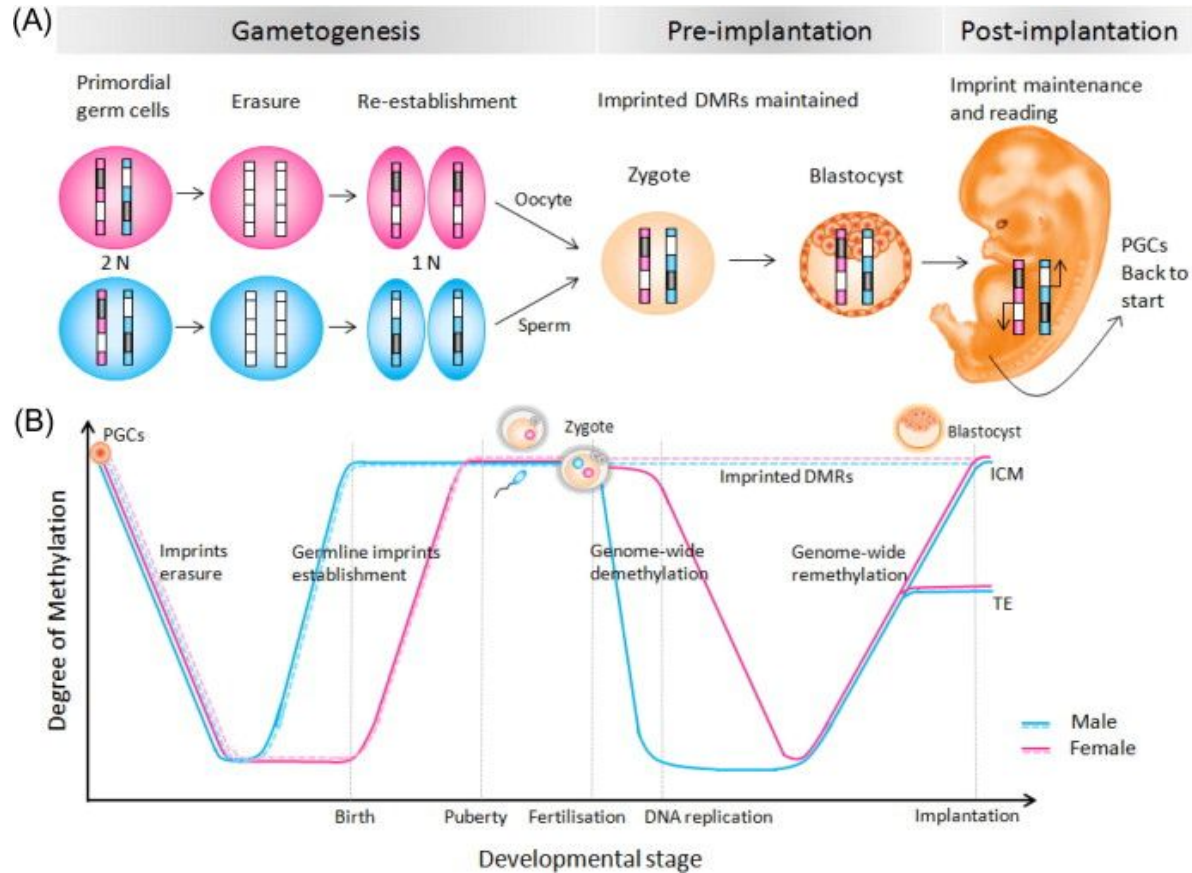


# X chromosome inactivation



Sado T, Okano M, Li E, Sasaki H. De novo DNA methylation is dispensable for the initiation and propagation of X chromosome inactivation. *Development*. 2004 Mar;131(5):975-82.

# Methylome erasure



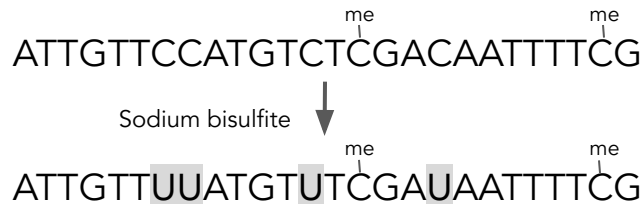
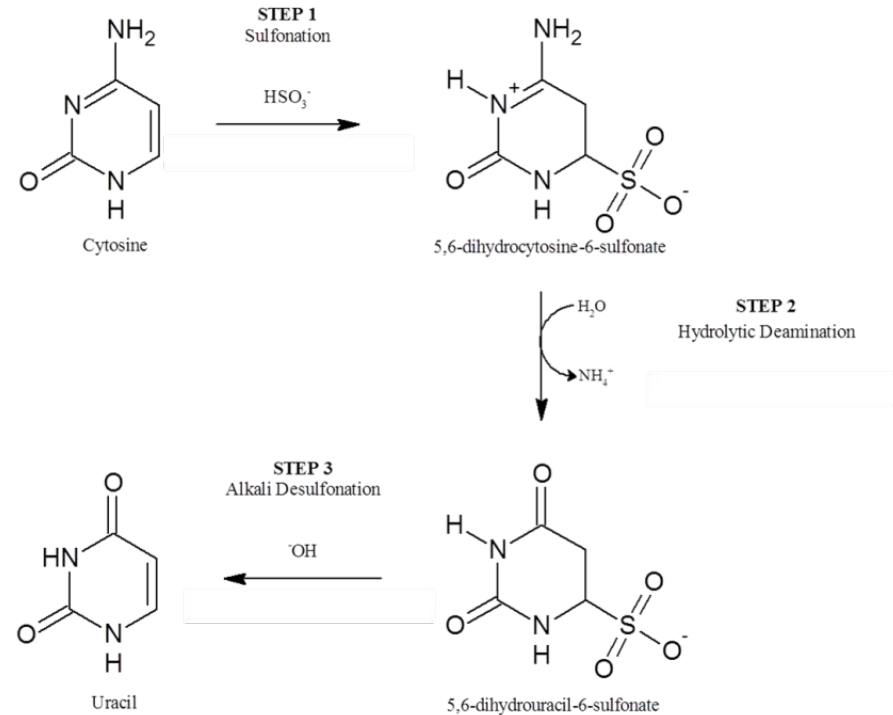


# Assaying DNA methylation

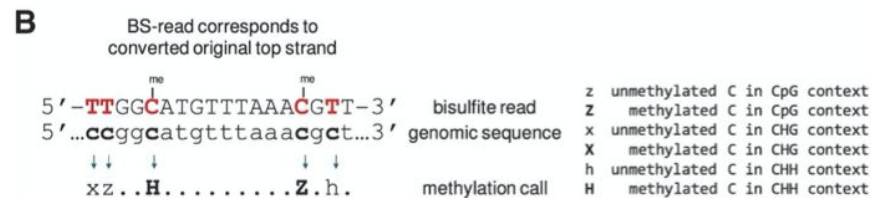
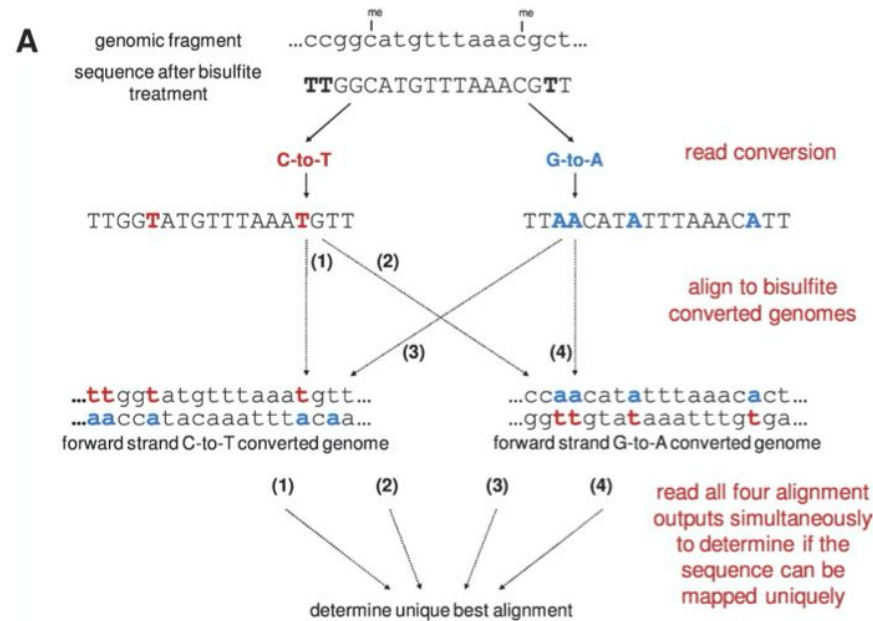


# Bisulfite treatment

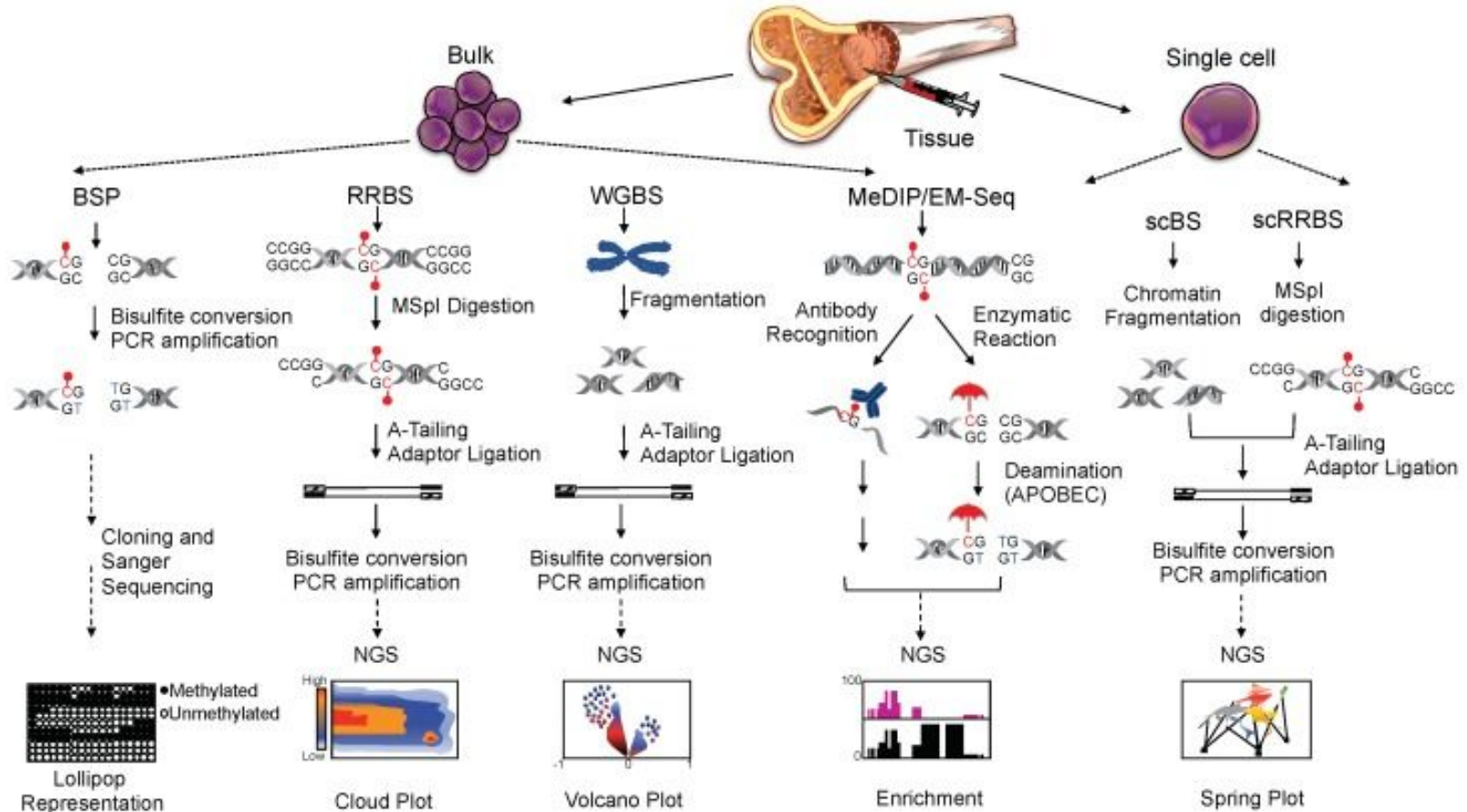
- Sodium bisulfite treatment of DNA causes unmethylated Cytosines to become Uracils
- Methylated CpGs are unaffected



# Bisulfite sequencing and mapping

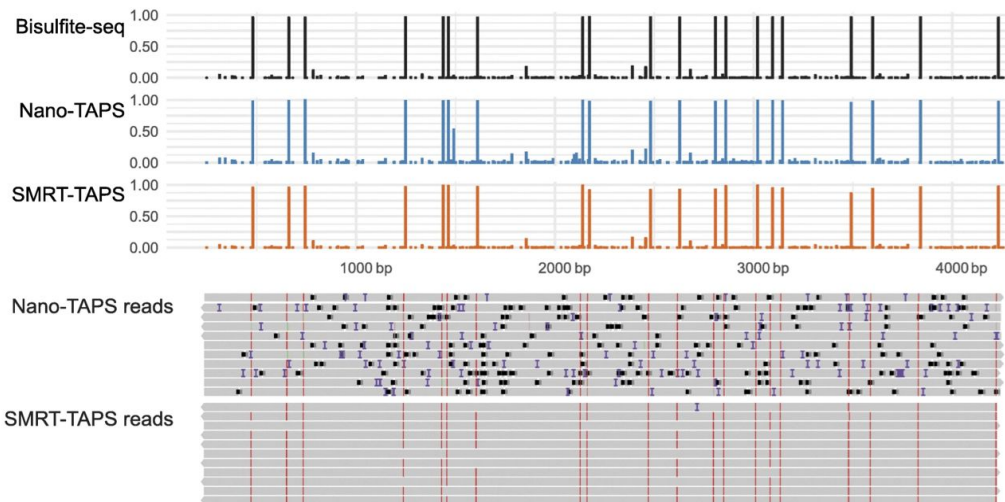
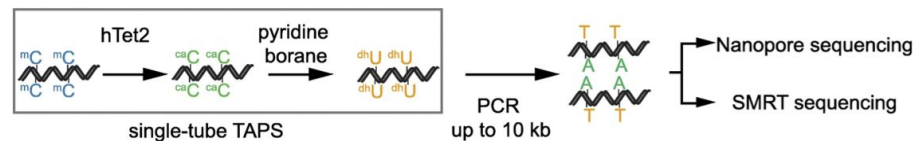
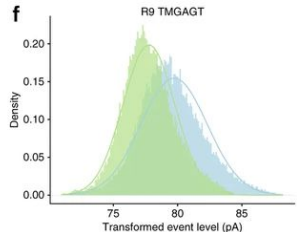
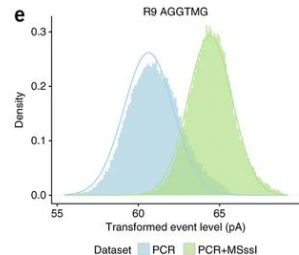
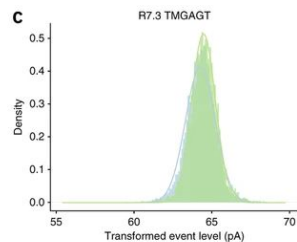
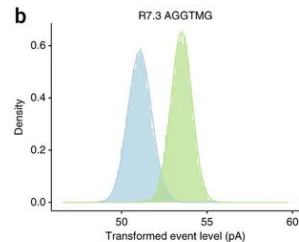
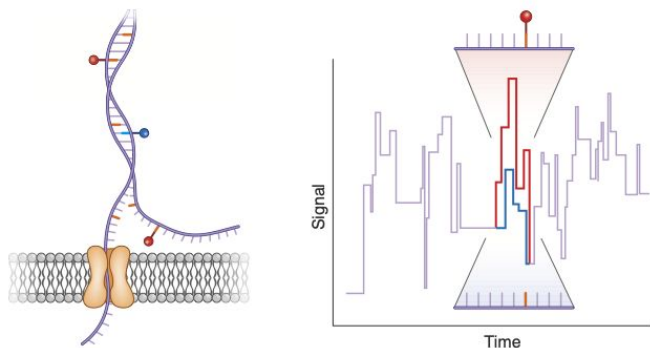


# Additional methylation assays



# Direct sequencing of methylation

Schatz, M. C. (2017). Nanopore sequencing meets epigenetics. *Nature Methods*, 14(4), 347–348.



Liu, Y., Cheng, J., Siejka-Zielińska, P., Weldon, C., Roberts, H., Lopopolo, M., Magri, A., D'Arienzo, V., Harris, J. M., McKeating, J. A., & Song, C.-X. (2020). Accurate targeted long-read DNA methylation and hydroxymethylation sequencing with TAPS. *Genome Biology*, 21(1), 54.

Simpson, J. T., Workman, R. E., Zuzarte, P. C., David, M., Dursi, L. J., & Timp, W. (2017). Detecting DNA cytosine methylation using nanopore sequencing. *Nature Methods*, 14(4), 407–410.

# Assignment data

Overview of early development (E3.5-E7.5)

