

# Epigenetics

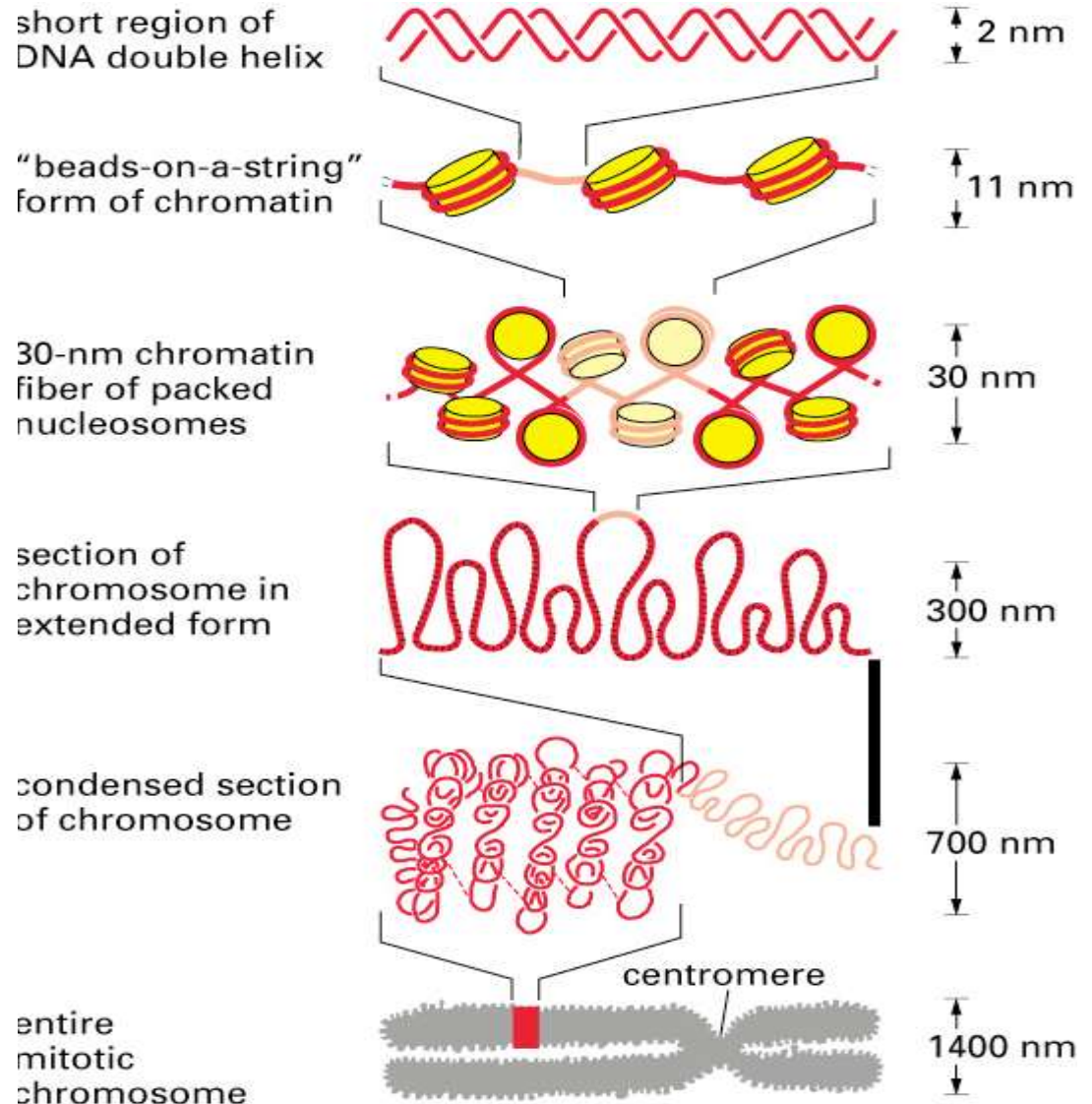
Epigenetics represents the science for the studying heritable changes of DNA, not involving changes in DNA sequence, that regulate gene expression.

There are at least two forms of information in the genome of the cell:

- A- Genetic information: provides the building block for the manufacture of all Proteins needed for the cell functional activity.
- B- Epigenetic information: provides additional instruction on how, when and where these information should be used.

## Chromatin Organization

Multiple Levels of packing are required to fit the DNA into the cell nucleus



NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 10,000-FOLD SHORTER THAN ITS EXTENDED LENGTH

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

The **nucleosome** consists of **146bp of DNA** wrapped around a protein core of 8 histones

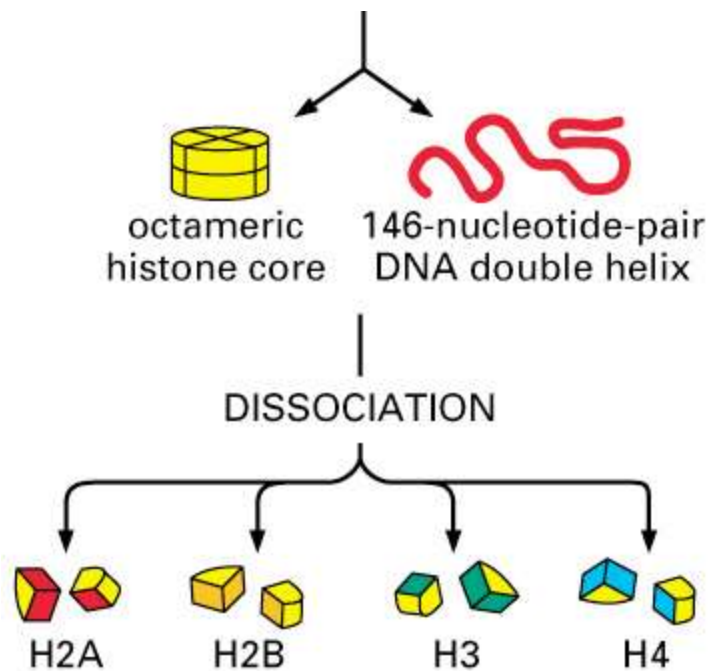


Figure 4–24 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Histone octamers assemble from pairs of dimers

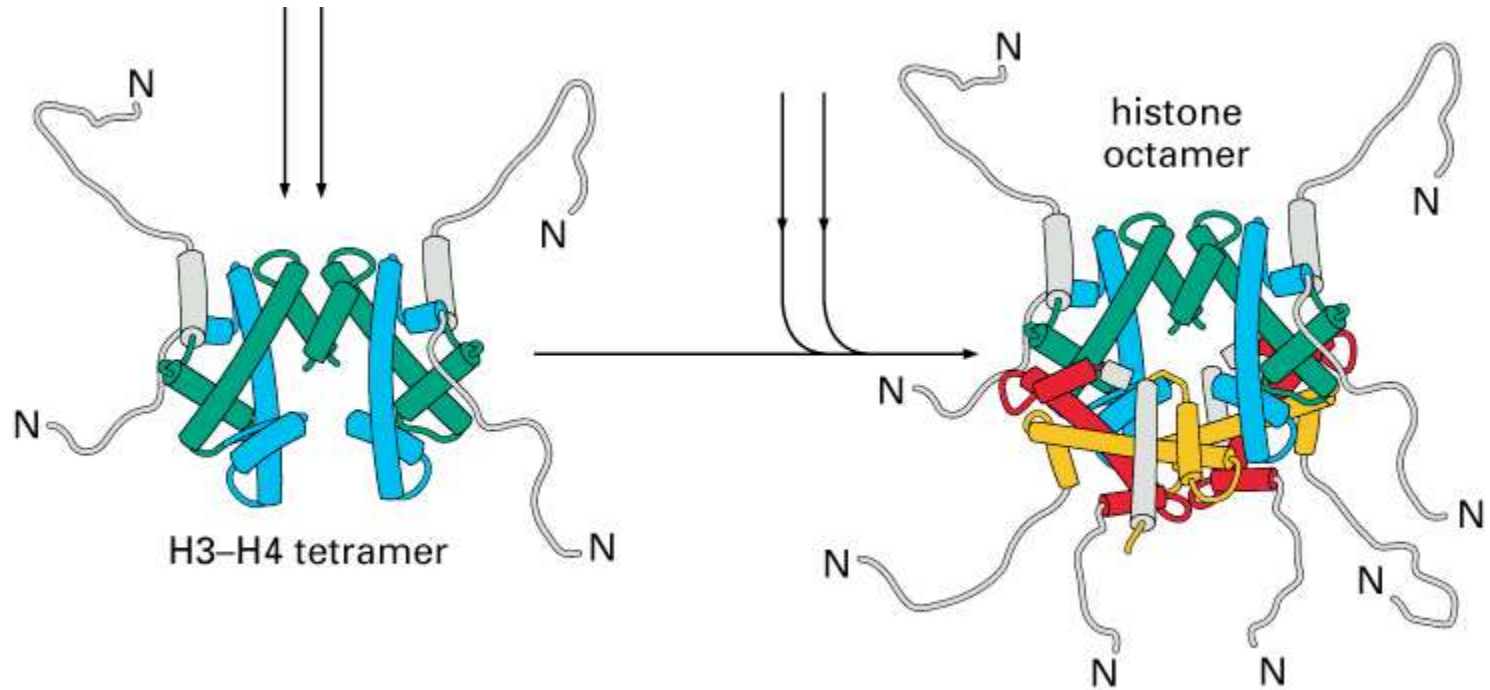


Figure 4-27 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Histone H1 helps compact the nucleosomes into the 30nm fiber

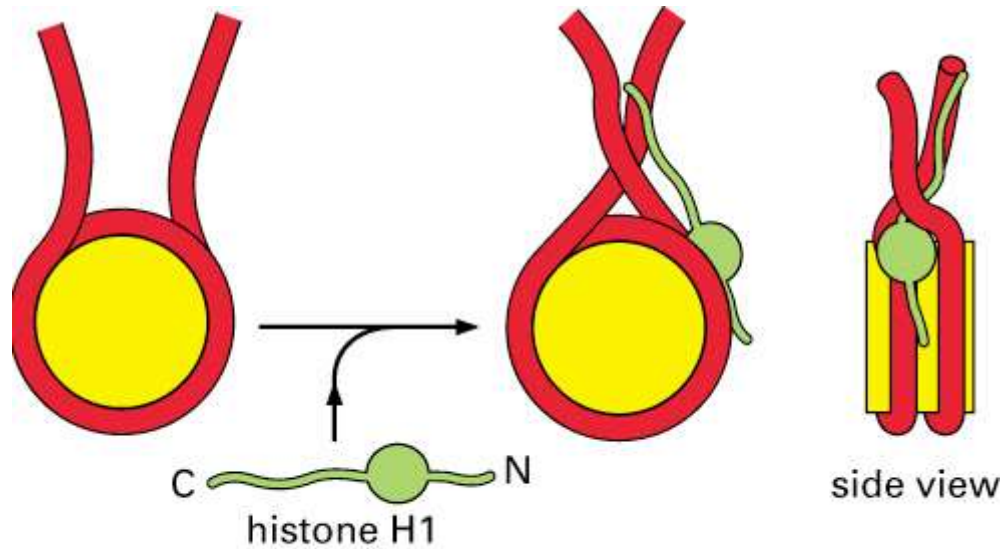


Figure 4-31 Molecular Biology of the Cell, 4th Edition

Other DNA binding proteins create irregularities in the structure of the 30nm fiber

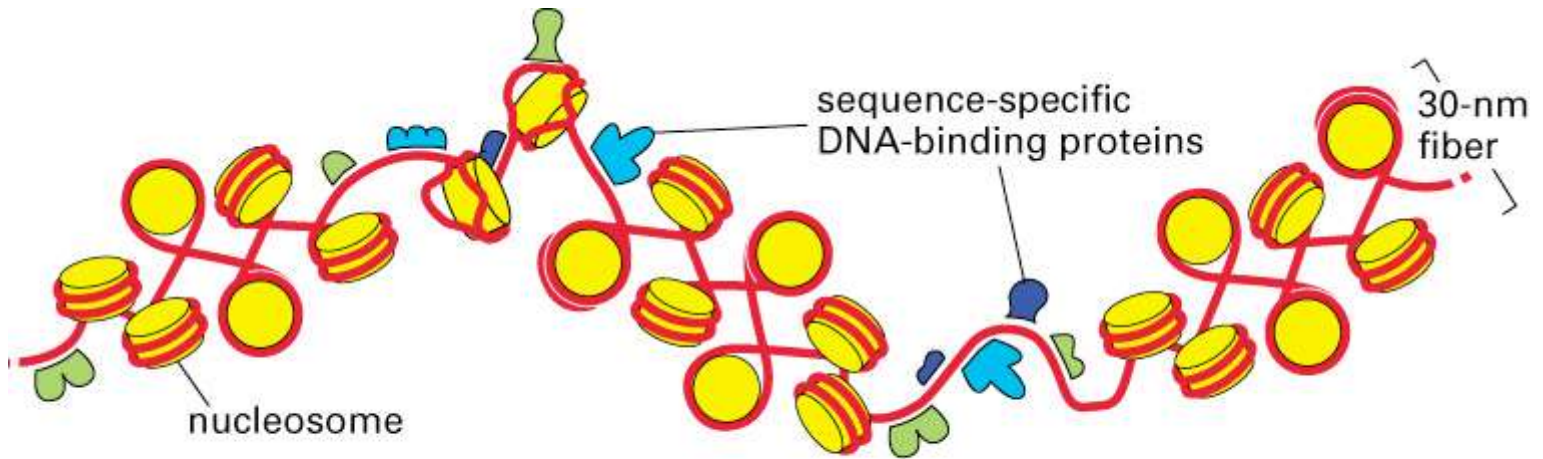
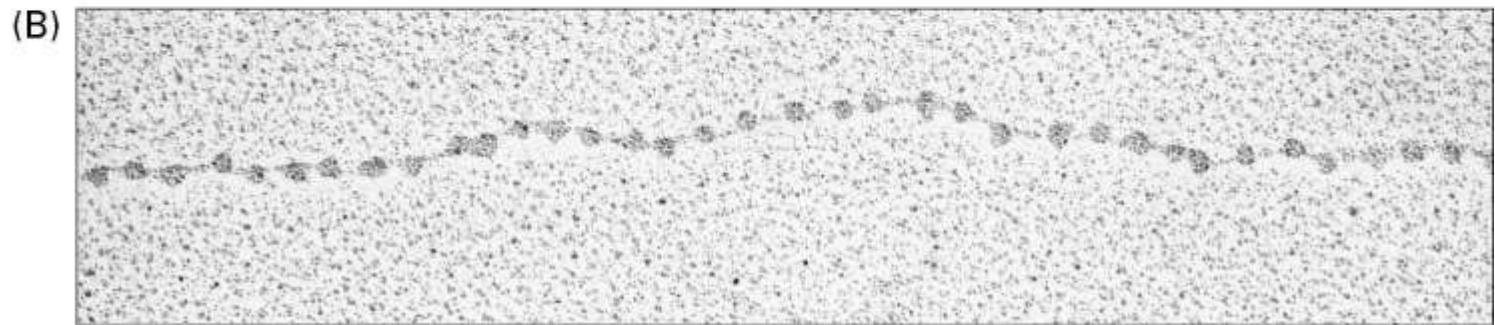


Figure 4-30. Molecular Biology of the Cell, 4th Edition.



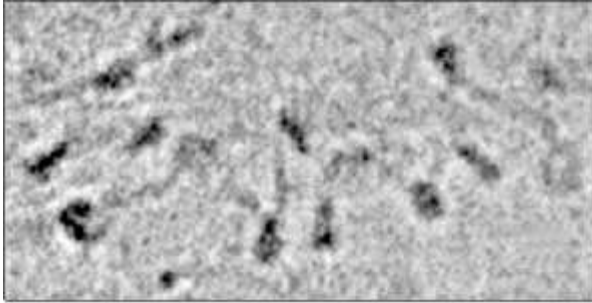
A = 30nm fiber of an interphase chromosome

B = Nucleosomes along a strand of DNA

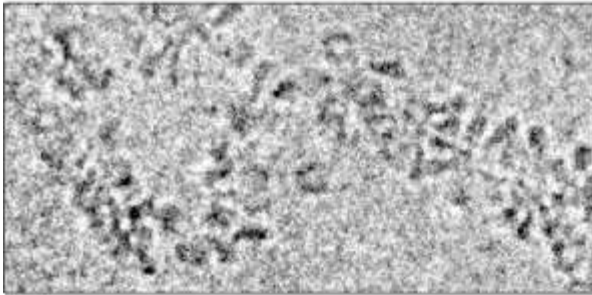
50 nm



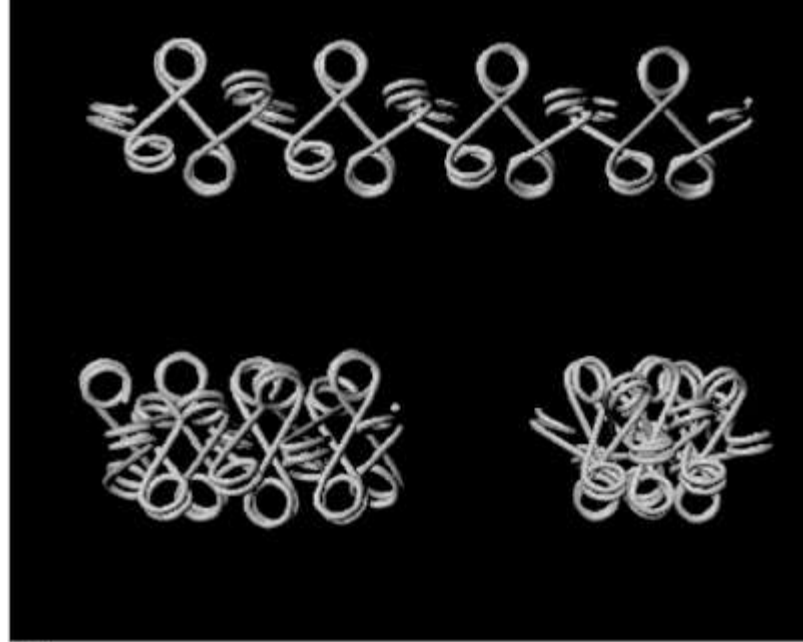
Nucleosomes pack together to create the 30nm chromatin fiber



(A)

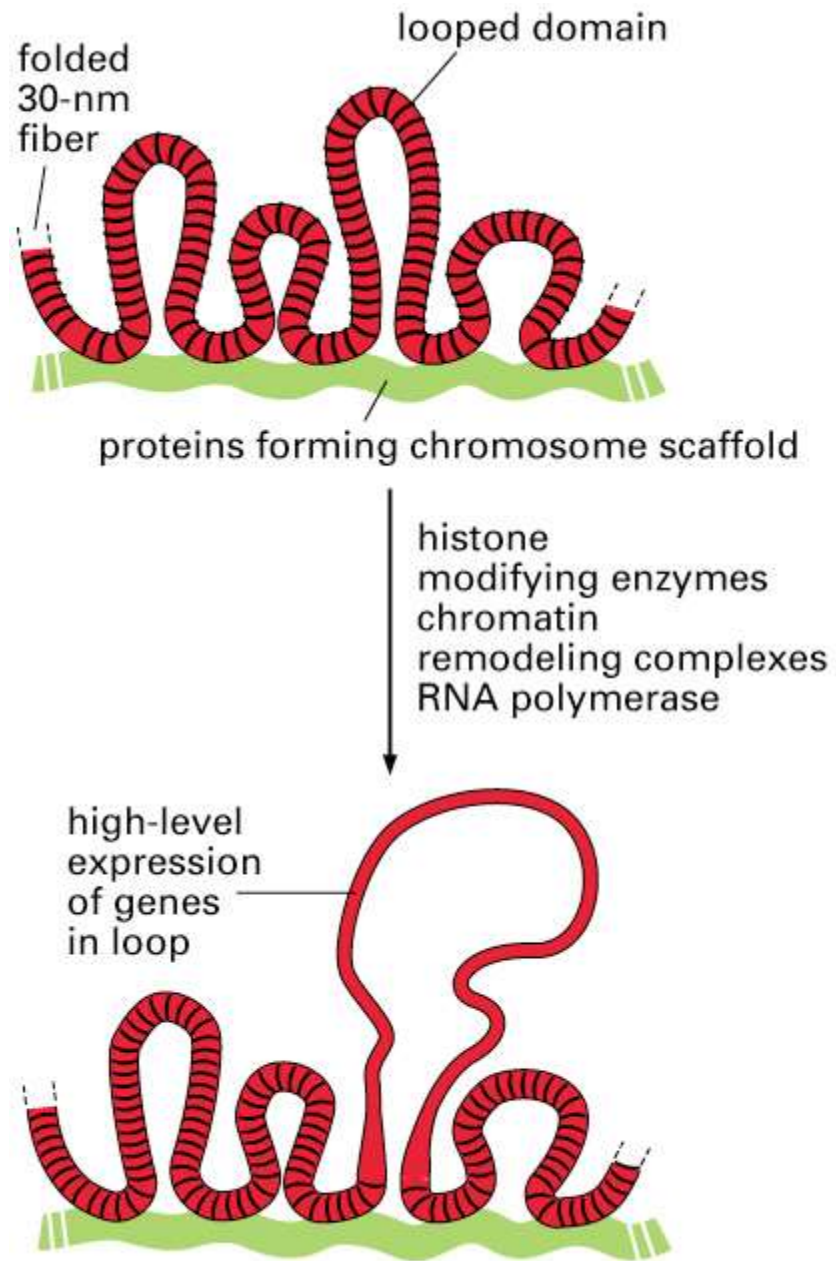


(B)



(C)

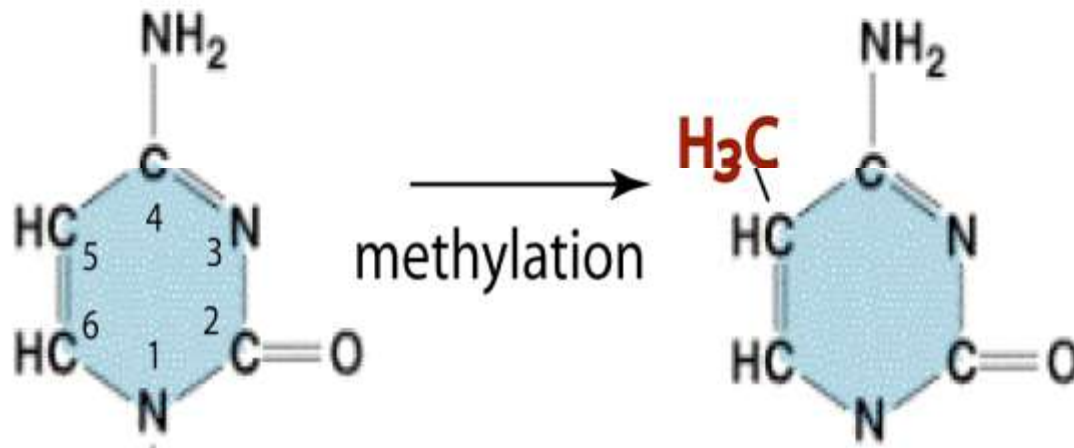
The 30nm fiber is organized to loops that can be opened up individually



This allows individual genes and sets of genes to be accessed without a global unpacking of the chromosome

Figure 4-44. Molecular Biology of the Cell, 4th Edition.

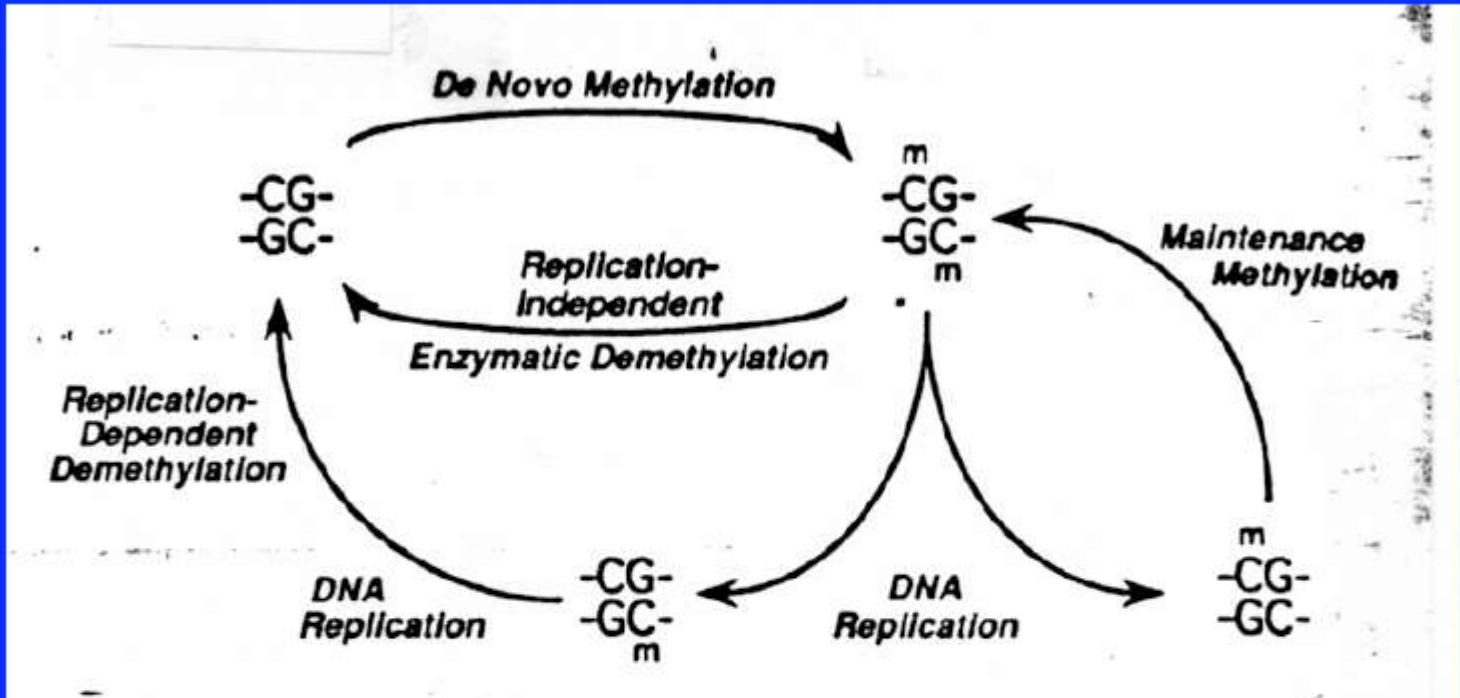
## DNA Methylation



DNA methylation occurs at 5MC within CpG dinucleotides.

5MC constitutes <1% of nucleotides

# DNA Methylation



**Figure 1.** *De novo* methylation, demethylation and maintenance methylation of DNA in mammals. The various pathways of methylation and demethylation found in mammals are shown schematically for a paired CpG dinucleotide. Methylation is indicated by a lower-case letter 'm'.

# **Methylation**

## **1. De Novo methylation.**

Some evidence that repeats may alter chromatin structure and signal de novo methylation.

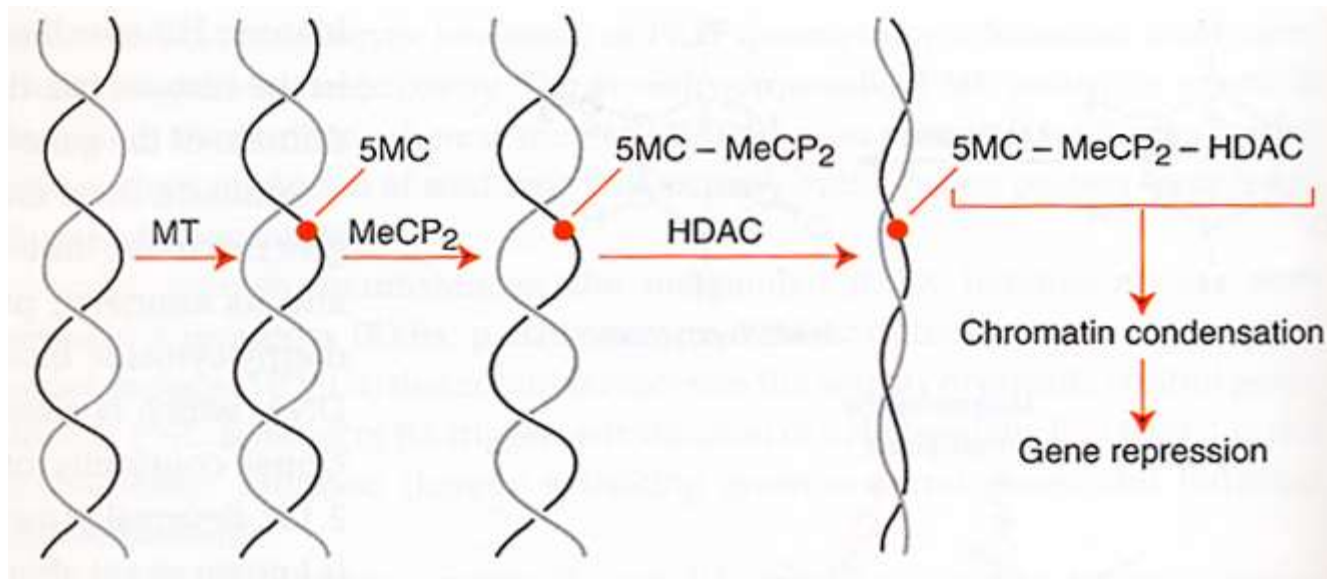
## **2. Maintenance Methylation- copies DNA so that**

methylation pattern on newly replicated DNA strand is

identical to previous.

## **3. Demethylation of DNA**

The presence of 5-methylcytosine leads to the silencing of genes in that local area of the chromosome



MT = DNA methyltransferase HDAC = Histone  
MeCP<sub>2</sub> = Methyl-CpG-binding protein Deacetylase

# Histone code hypothesis

Histone Tails are subject to a variety of covalent modifications

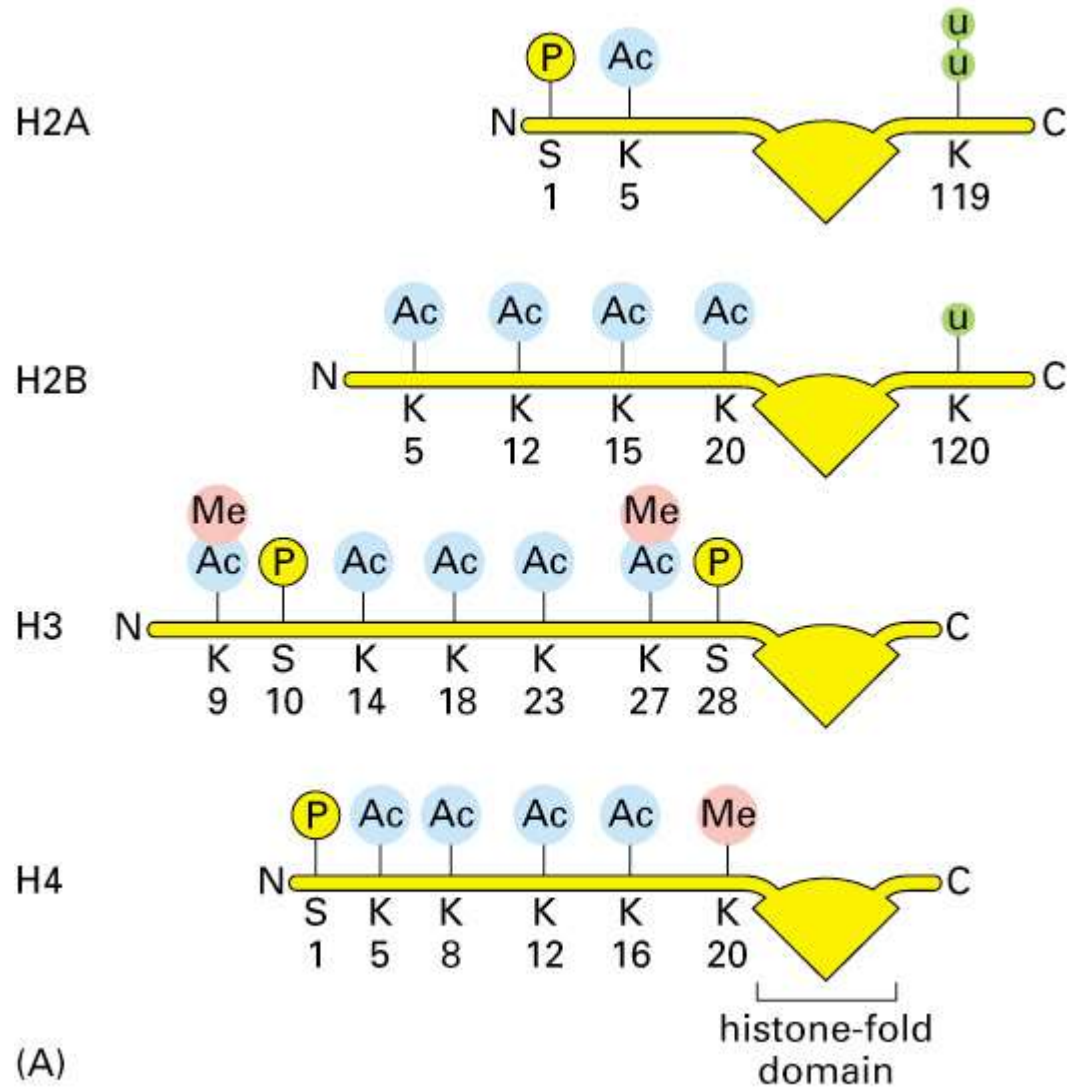


Figure 4-35 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

## Enzymes providing histone modifications

- Acetylation: HATs - CBP,p300, GCN5, ATF2, Tip 60...
- Deacetylation: HDACs- class I and II
- Methylation:
  - Lysine : SET-domain HMTase and non-SET domain HMTase (Dot1)
  - Arginine: PRMT family, CARM1
- Demethylation: LSD1
- Ubiquitination: ubiquitin conjugase Rad6/ligase Bre1forH2B
- De-Ubiquitination: SAGA-associated Ubp10



# Histone Code hypothesis

- Modifications of the Histone tails act as marks that can be read by other proteins to control the expression or replication of chromosomal regions.
- The coding in the histones may be heritable.
- Generally, histone acetylation is associated with transcriptionally active genes
- Deacetylation is associated with inactive genes (= gene silencing)