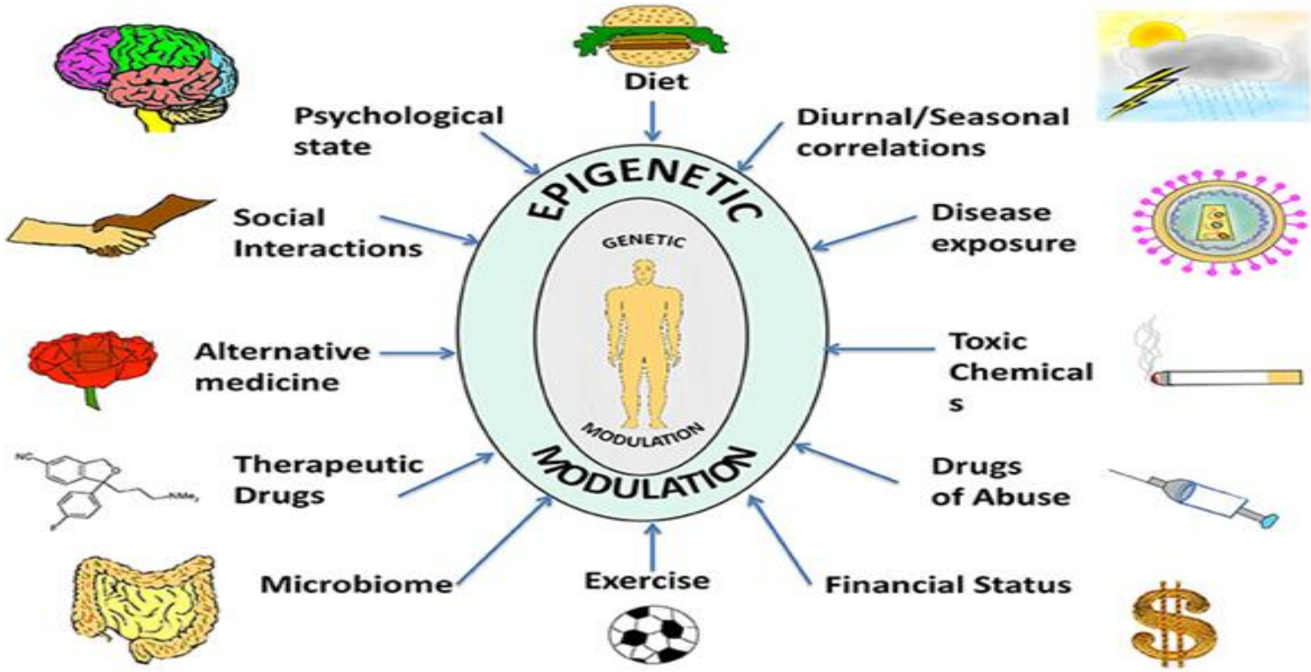
Epigenetics

- The term "Epigenetics" was coined by C.H. Waddington in 1942.
- Literally Epigenetics means "above" or "on top of" genetic information. It refers to external modifications to DNA that turn genes "on" or "off." These modifications do not change the DNA sequence, but instead, they affect how cells "read" genes.
- Definition: It is the study of the changes in gene expression that are heritable but does not involve any change in the underlying DNA sequence. *"A change in phenotype without a change in genotype"*
- *For example: Monozygotic Twin…..Genome is identical but phenotype is different*
- The epigenetic modifications/changes are regular and occur naturally but may also be influenced by various factors such as age, environment, lifestyle, and disease state.
- These epigenetic modifications can make the changes in the cells to finally differentiate as skin cells , liver cells, brain cells etc.
- For example, epigenetic modifications control how and when certain genes are turned on and off to help the body grow and develop

Or

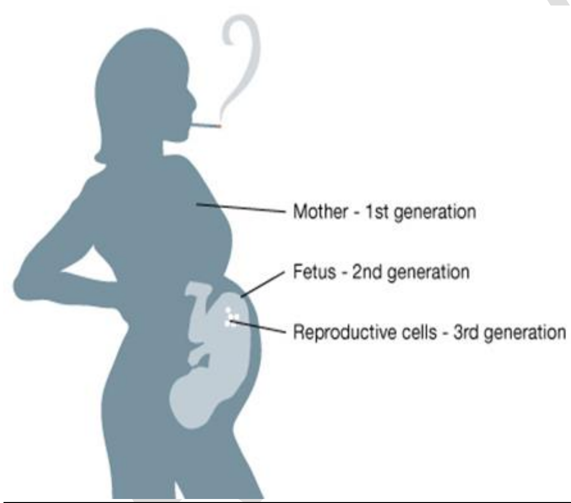
- They can have damaging effects and result in diseases like cancer, arthritis etc.



Nature of Epigenetic modifications

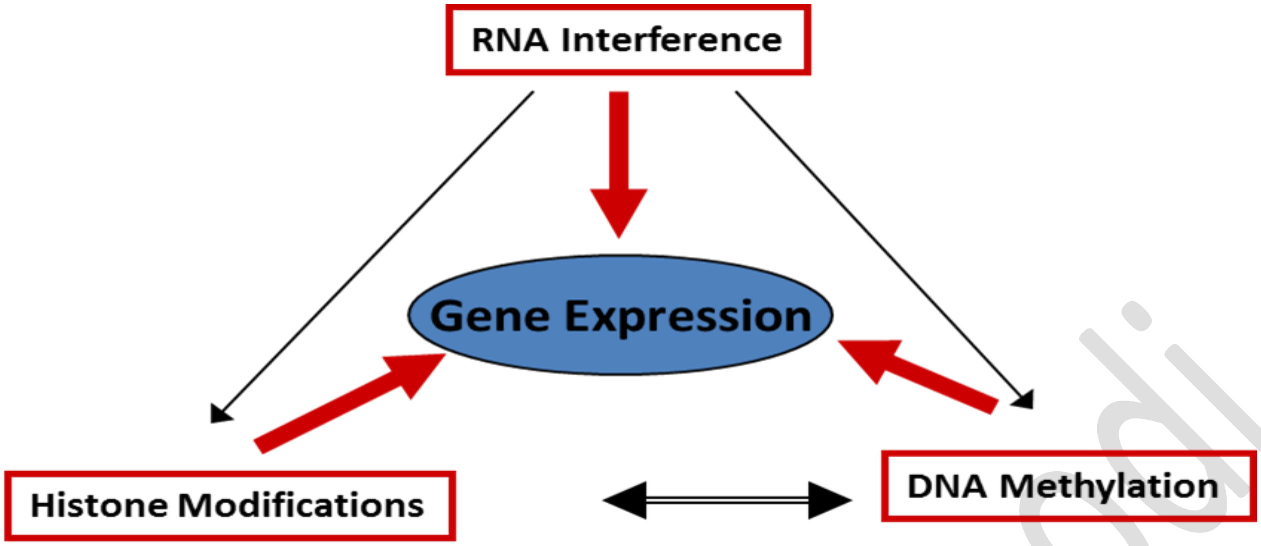
1. Stable: Passed on to future generations

2. Dynamic: Epigenetic modification can change in response to environmental stimuli. For example Life style, eating habits etc



The Epigenetic changes/modifications occur by three process:

1. DNA methylation 2. Histone modification 3. Non coding RNA



<u>1-Methylation</u>:- methylated cytosines in CCGG sequences for genes non in transcription phase as inactive X chromosome in mammalian cells (Bar Boddy), DNA sequence contain CPG sequence called CPG islands. Methylated causes inactive gene ***What is CpG* dinucleotide?** *CpG* dinucleotide denotes a *5′—C—phosphate—G—3′* , that is, cytosine and guanine separated by only one phosphate.

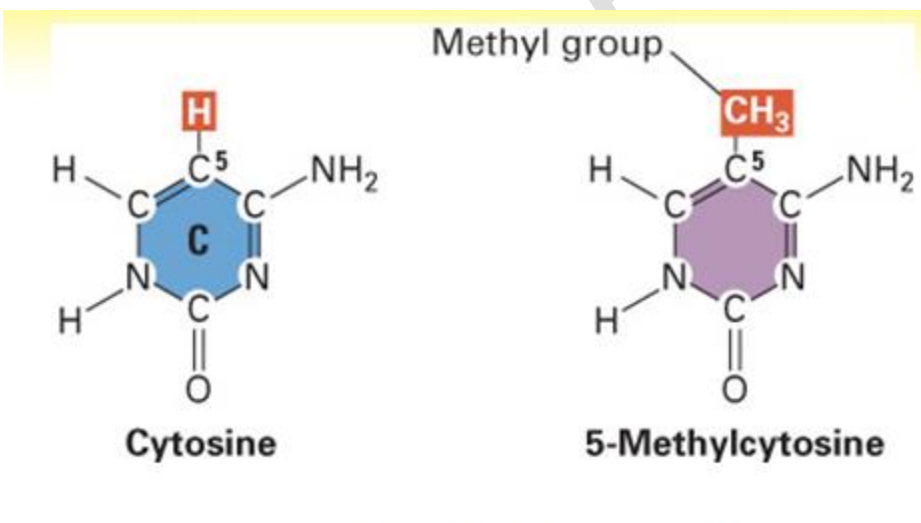
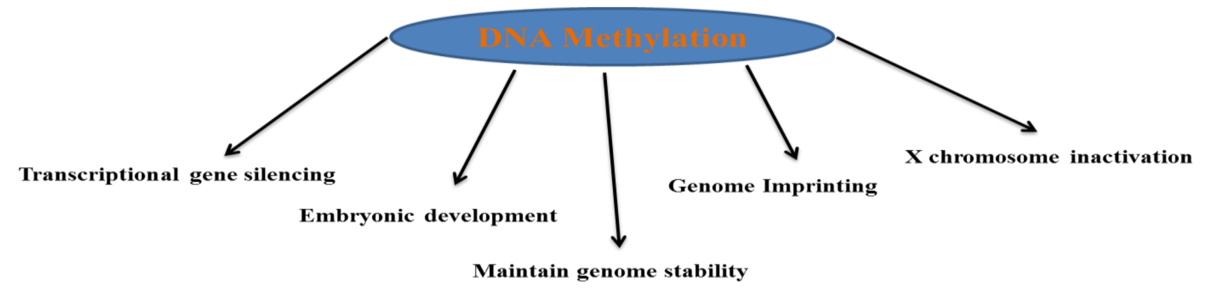


Figure 11.30: Structures of cytosine and 5-methylcytosine.

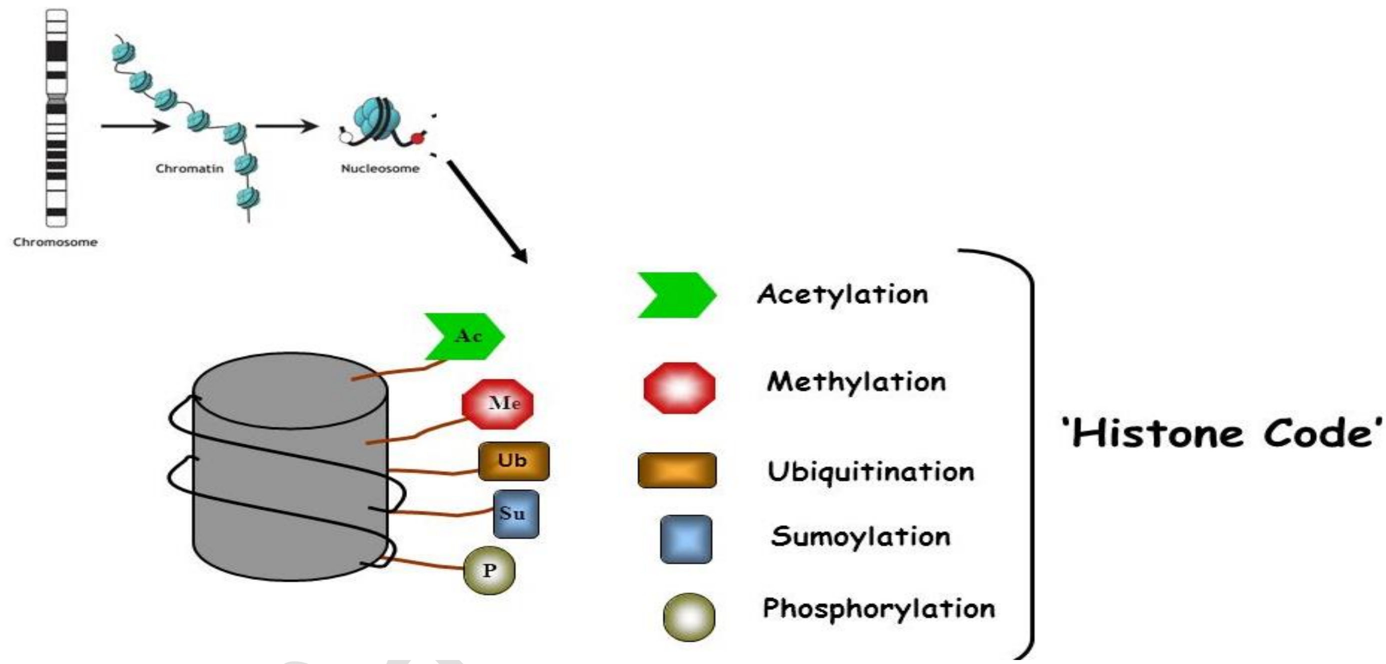
<u>Important Functions of DNA Methylation</u>



➢ What are the factors that can affect DNA Methylation ؟Aging , Nutrient intake, . Genetic, Metal exposure, Tobacco Smoking, Alcohol Drinking

2-Histone Modification

A histone modification is a covalent post-translational modification (PTM) to histone proteins which includes :- Methylation, Phosphorylation, Acetylation, Ubiquitylation, Sumoylation



Histone modifications function in different biological processes such as

- Transcriptional activation
- Transcriptional inactivation
- Chromosome packaging
- DNA damage/repair.

These post-translational modification in the histones protein can effect gene expression by changing chromatin structure or recruiting histone modifiers.

3-Non coding RNA

A non-coding RNA (ncRNA) is a functional RNA molecule that is transcribed from DNA but not translated into protein.

Epigenetics related ncRNAs include:

micro RNA (miRNA)

1) Small interfering RNAs (siRNA),
2) Long non-coding (lncRNA) and
3) Piwi-interacting RNAs (piRNA).

Non coding RNAs (ncRNAs) involved in epigenetic processes is divided into two main groups;

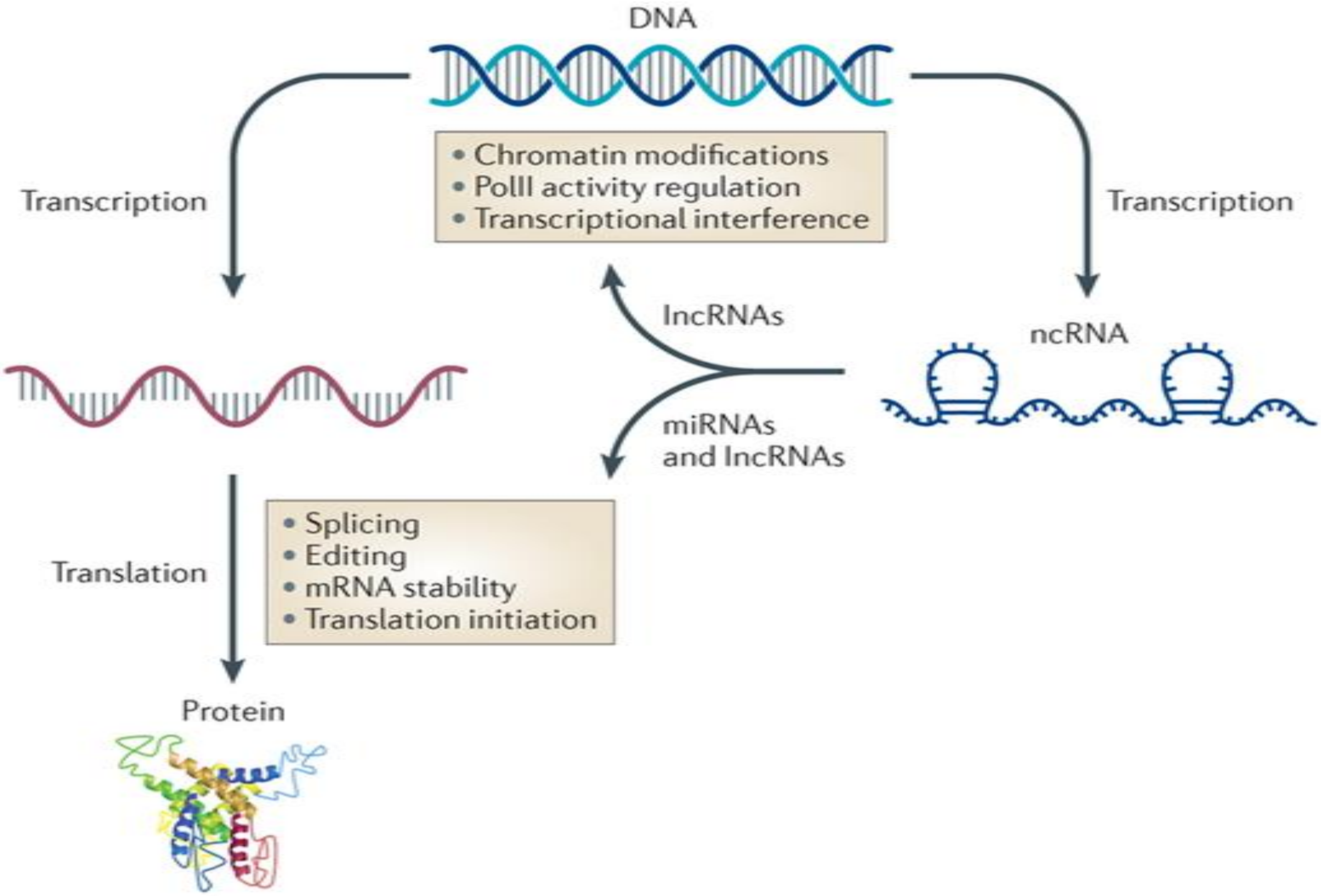
1. The short ncRNAs (<30 nts)
2. The long ncRNAs (>200 nts).

The three major classes of short non-coding RNAs are

1. MicroRNAs (miRNAs)
2. Short interfering RNAs (siRNAs),
3. Piwi-interacting RNAs (piRNAs).

Functions of Non coding RNA

Non coding RNA are plays important role in :- Heterochromatin formation, Histone modification, DNA methylation targeting, Gene silencing.Control gene expression at the transcriptional and post transcriptional level.



The two classic epigenetic processes that causes disease when they are not properly regulated in mammals are ; 1. Genomic imprinting: 2. X chromosome inactivation:

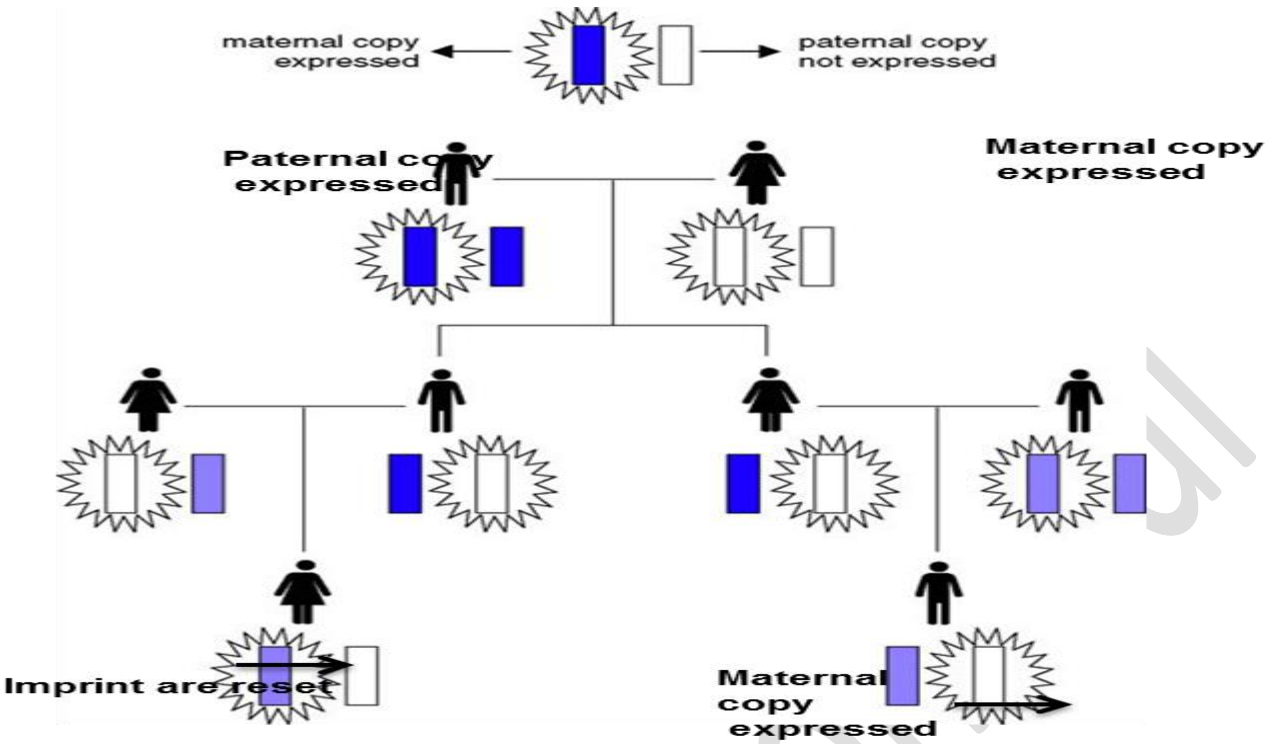
Genomic imprinting: It is an epigenetic process that involves DNA methylation and histone modification without changing the genetic sequence.

- In genome imprinting certain genes are expressed in a parent-of-origin-specific manner.
- Imprinted gene follows Non- Mendelian inheritance pattern.
- Imprinting plays important role in determining the inheritance of certain genetic diseases.

For example:

- If the allele inherited from the father is imprinted, it is thereby silenced, and only the allele from the mother is expressed.
- OR If the allele from the mother is imprinted, then only the allele from the father is expressed.
- Imprinted genes are reset in the germ cells. For example If a mutant gene is imprinted, sex of

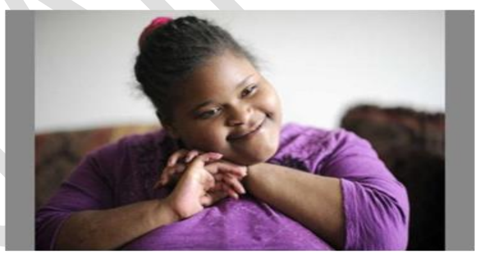
the parent it was inherited from plays a role in the expression of the disease phenotype



For example Angelman syndrome and Prader–Willi syndrome are due to small deletion in chromosome 15. If it is inherited from father it causes Prader–Willi syndrome.

If it is inherited from Mother it causes Angelman syndrome


Angelman syndrome


Prader–Willi syndrome

Epigenetic modifications (also known as epigenetic marks) have a control on many normal functions of cells in our bodies. For example, certain genes normally work to protect against cancer., but some epigenetic marks can turn these genes off, increasing the risk of cancer

Certain diseases and conditions that are linked to epigenetic or developmental epigenetic changes are:

Obesity, Heart disease, Various cancers, Autism, Fragile X syndrome.

- **Epigenetic modifications are good therapeutic candidates because**;

1) They control transcriptional activity and they are somatically heritable.
2) Epigenetic changes can precede disease pathology and thus are diagnostic indicators for risk.
3) It can also act as prognostic indicators for disease progression.

4) They are also used as target for chemotherapy For example: DNA methylation inhibitors