BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620 024
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Programme: M.Sc. Biochemistry

Course Title : Chromatin and Epigenetics
Course Code : BC205DCE

Unit-3
Epigenetic Modifications

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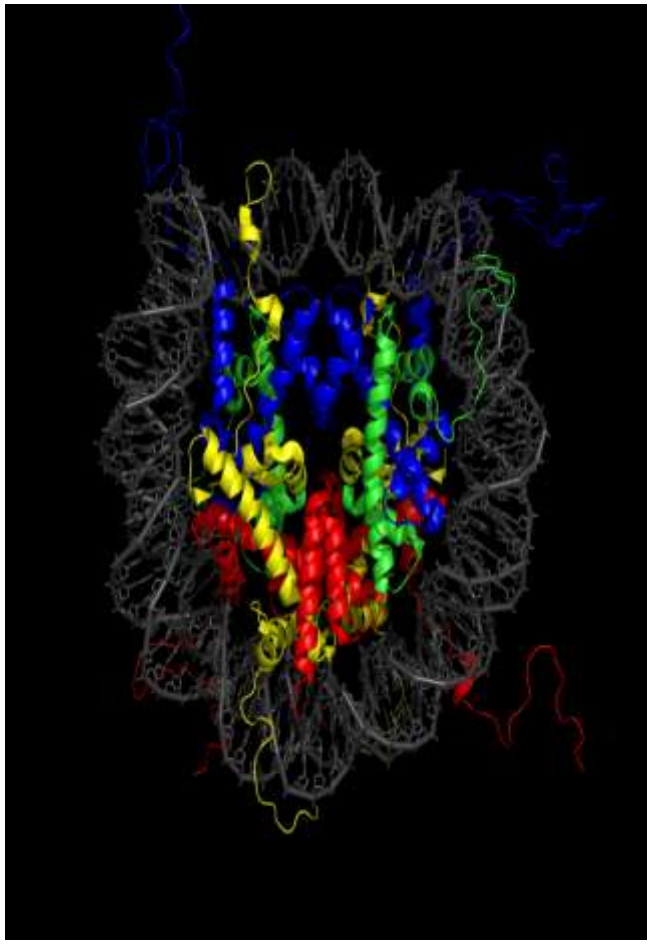
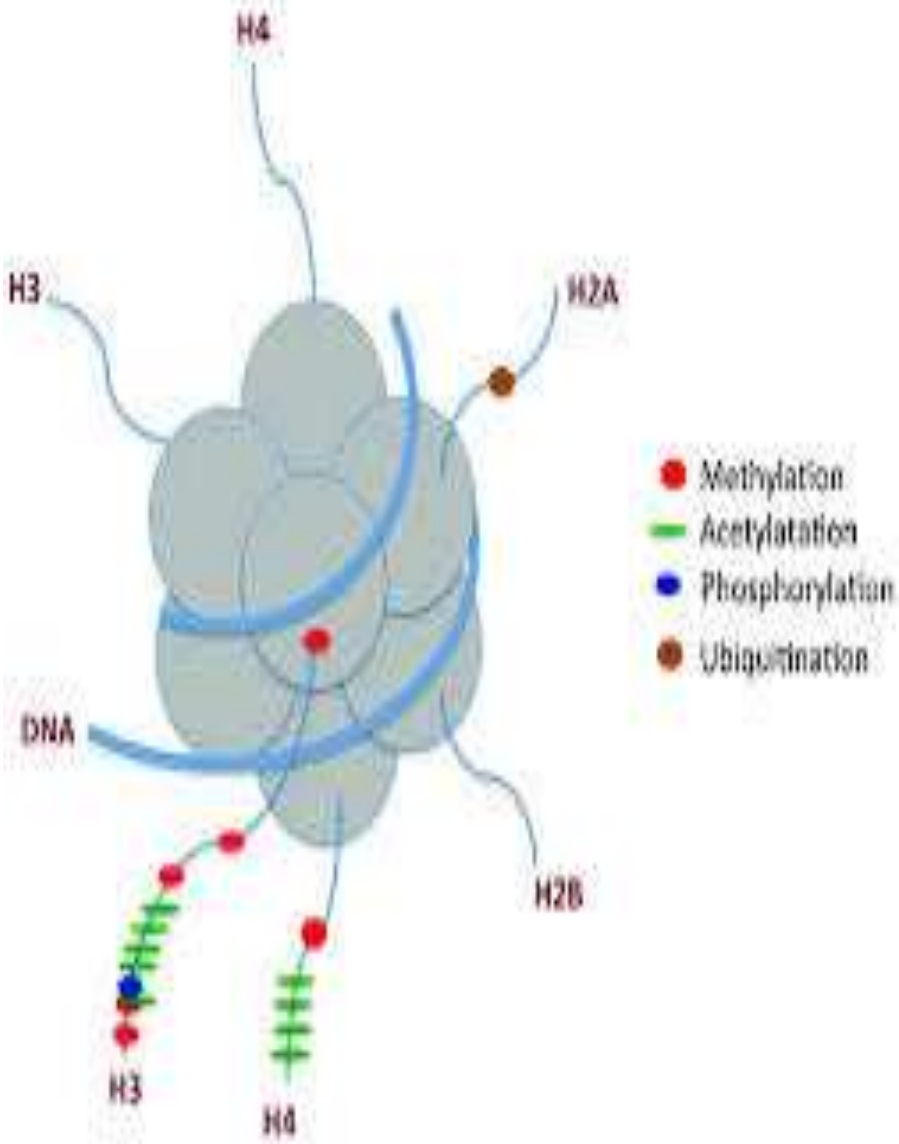
Unit-3 Overview

- Chromatin remodeling by DNA binding proteins
- SWI/SNF family repositioning nucleosomes
- Chromatin modifications by spontaneous conformational change
- Covalent modifications
- Epigenetic modifications
- DNA methylation
- Post translational modification of histones

Histone Modifications

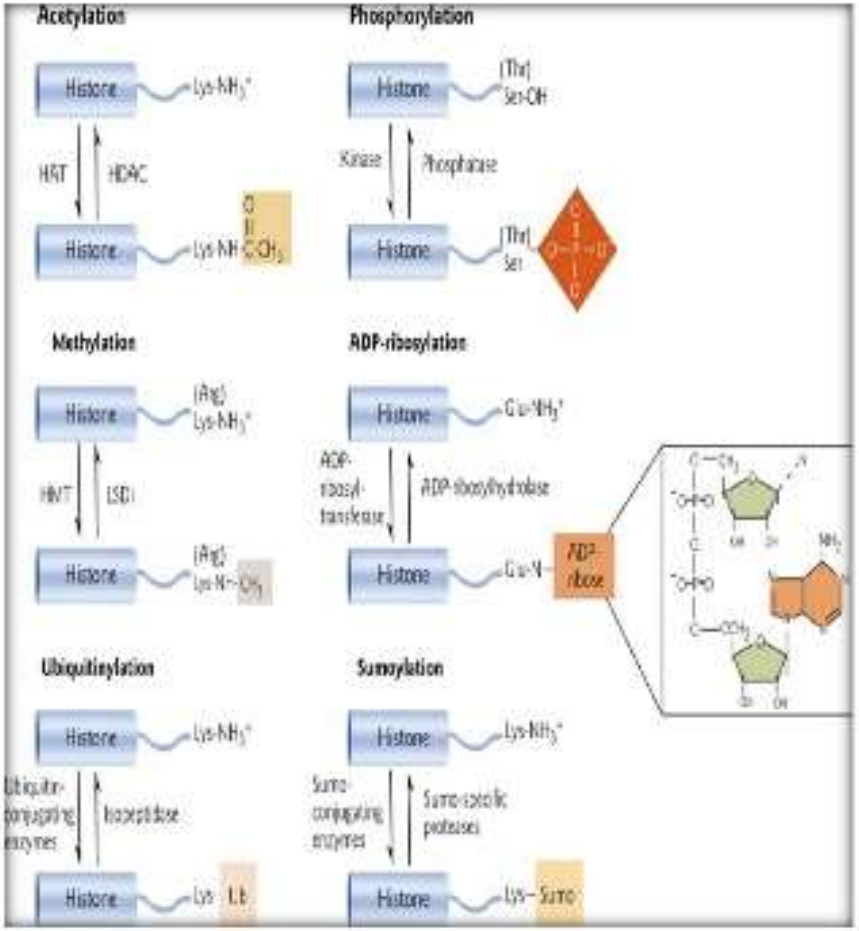




❑ Some Examples of Histone Modification and Modifiers

Amino acid Residue	Modification Type	Modiying Enzyme
Lysine	Acetylation Deacetylation	HAT HDAC
Lysine	Methylation Demethylation	HMT HDM
Lysine	Ubiquitylation Deubiquitylation	Ub ligase Ub protease
Serine/Threonine	Phosphorylation Dephosphorylatio n	Kinase Phosphatase
Arginine	Methylation Demethylation	PRMT Deiminase/De methylase

Others: Sumoylation (Lysine), ADP Ribosylation (Glutamate)

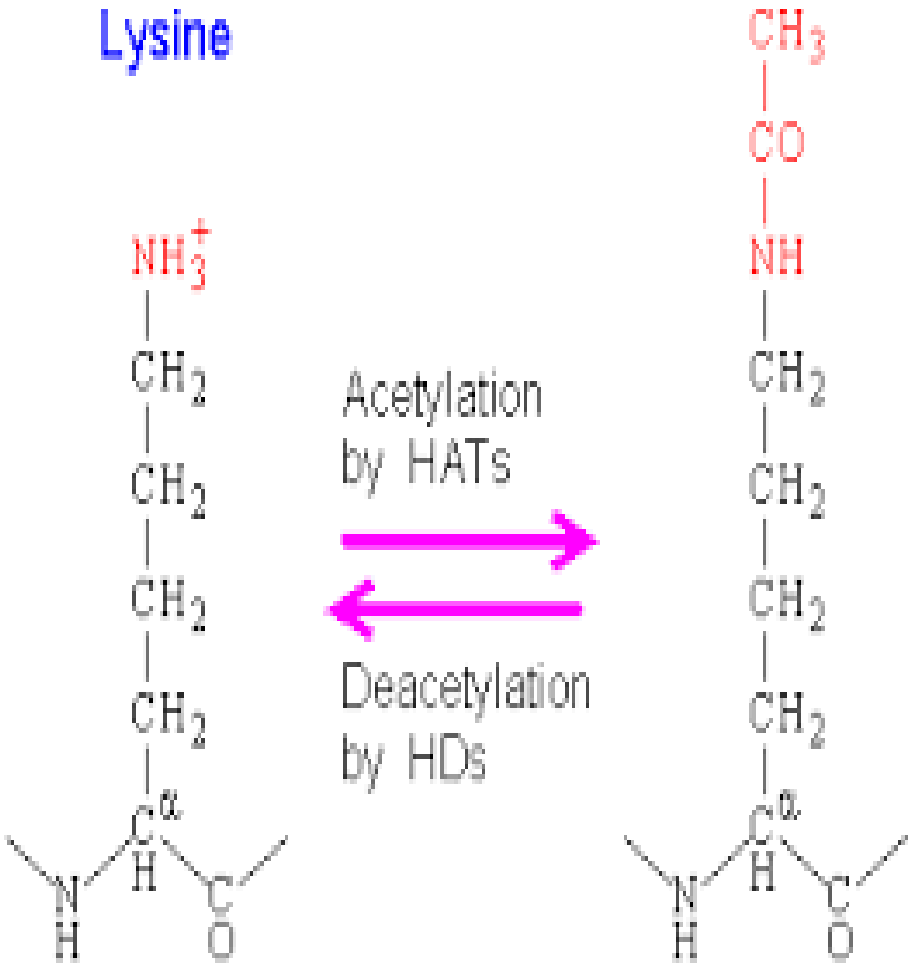


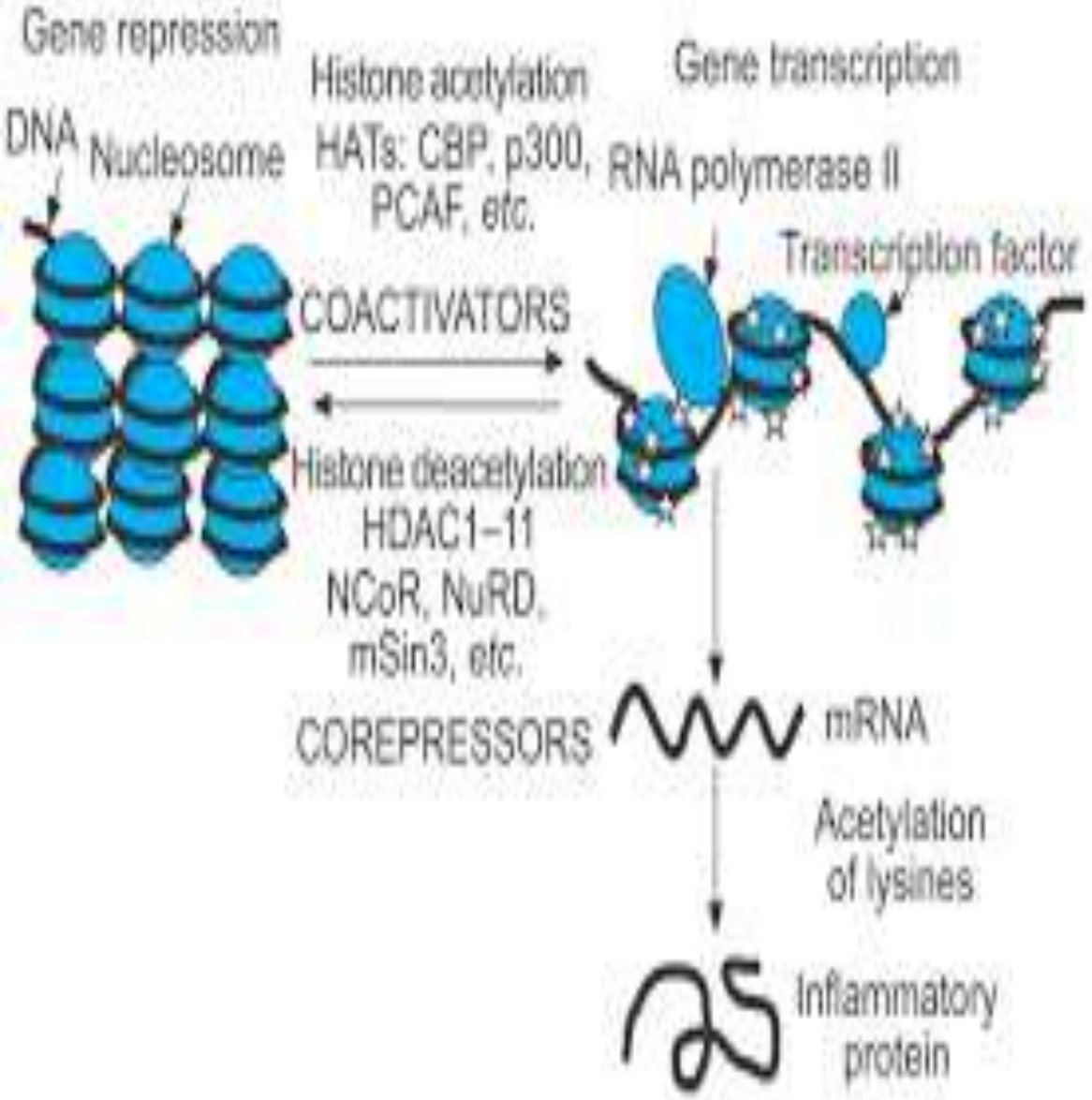
Post-translational Modification of Histone N-terminal Tails

CORE HISTONES

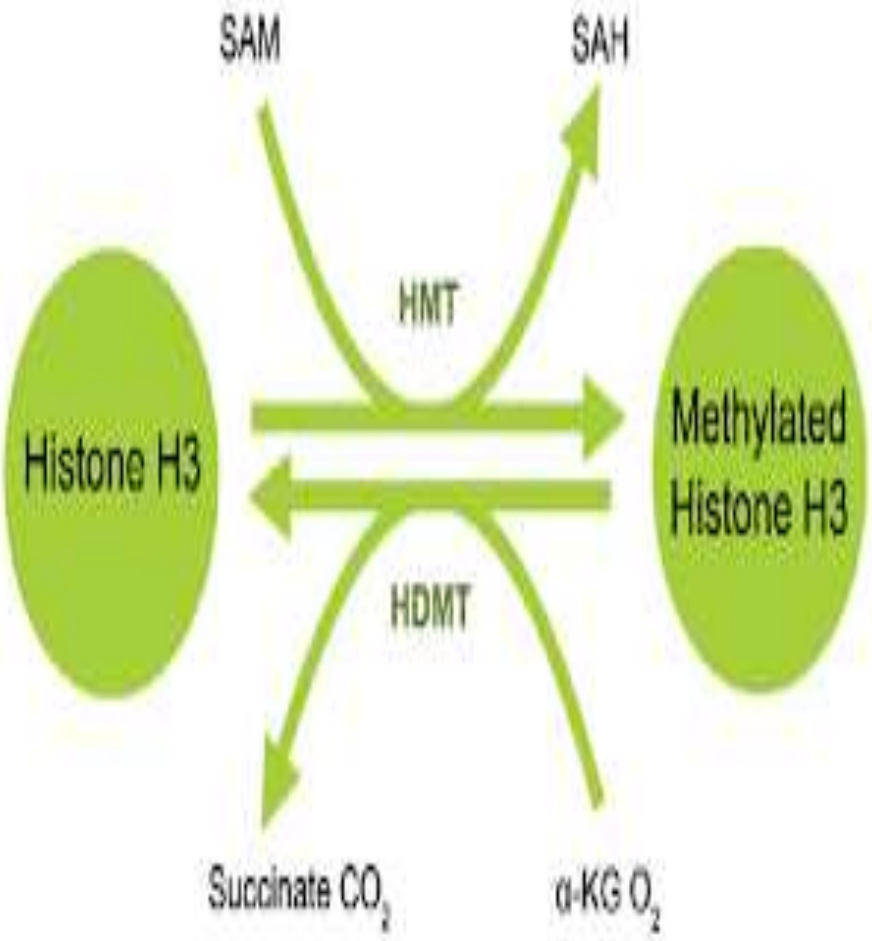
- In core histones following families are included.
- H2A} contain more lysine
- H2B}contain more lysine
- H3} contain more arginine
- H4} contain more arginine

Acetylation




Gene repression
DNA
Nucleosome
Histone acetylation
HATs: CBP, p300,
PCAF, etc.
COACTIVATORS
Histone deacetylation
HDAC1–11
NCoR, NuRD,
mSin3, etc.
COREPRESSORS
Gene transcription
RNA polymerase II
Transcription factor
mRNA
Acetylation
of lysines
Inflammatory
protein

Histone Methylation



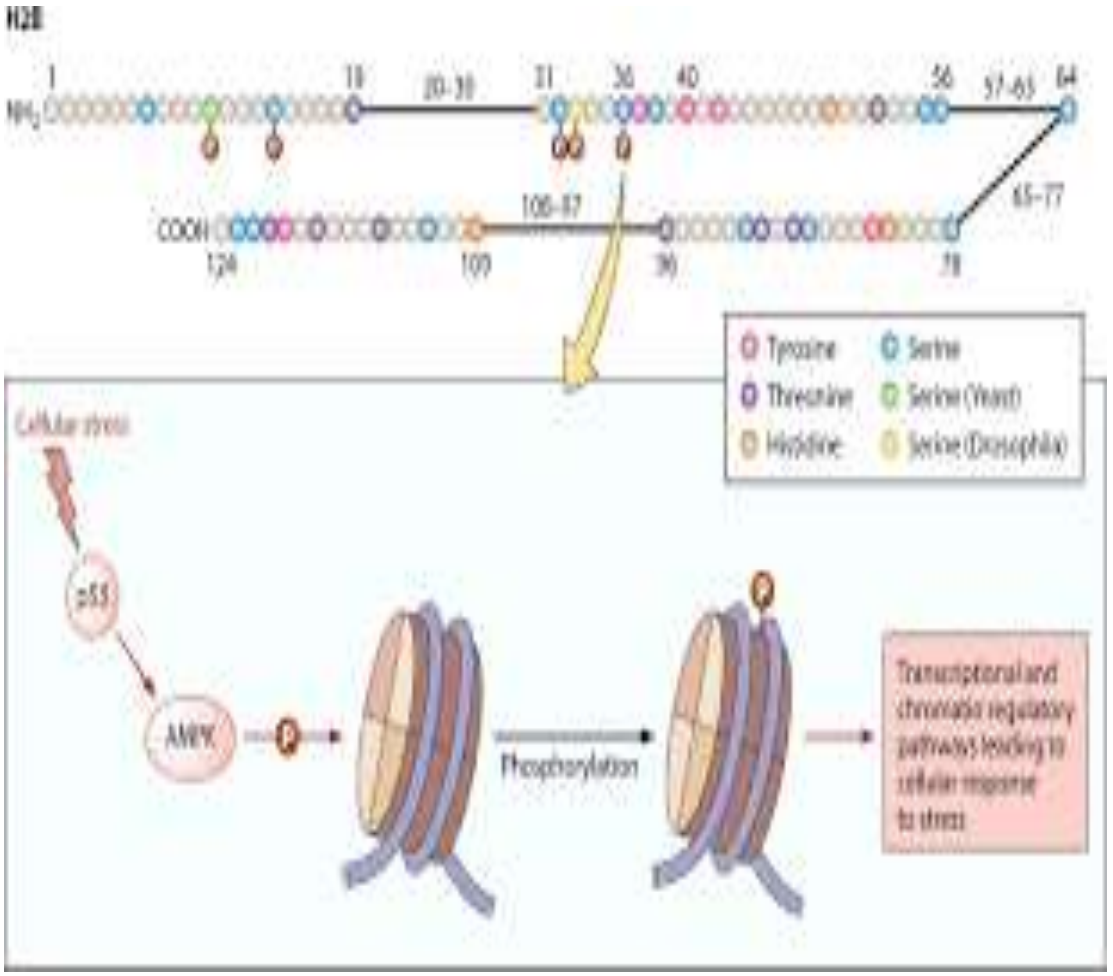
Arginine methylation promotes transcriptional activation while lysine methylation both transcriptional activation and repression depending on the methylation site.

Lysines can be mono-, di-, or tri-methylated

Methylation activation marker or repressive signals (K4 of histone H3 or K9 of histone H3)

permanent signal for heterochromatin formation (H3K9me3)

Histone phosphorylation



3. Phosphorylation

- Phosphorylation is the addition of a phosphate group (PO_4^{3-}) to a molecule.

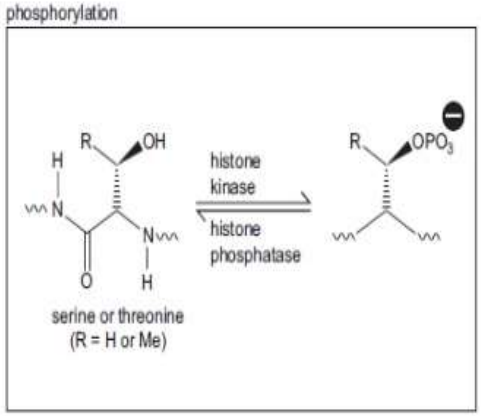
- Phosphorylation is catalyzed by various specific protein **kinases**, whereas **phosphatases** mediate removal of the phosphate group.

- Histones can also get phosphorylated and the most studied sites of histone phosphorylation are the serine 10 of histone H3 **(H3S10)** that is deposited by the **Aurora-B kinase** during mitosis.

❑ Role of histone phosphorylation in DNA repair

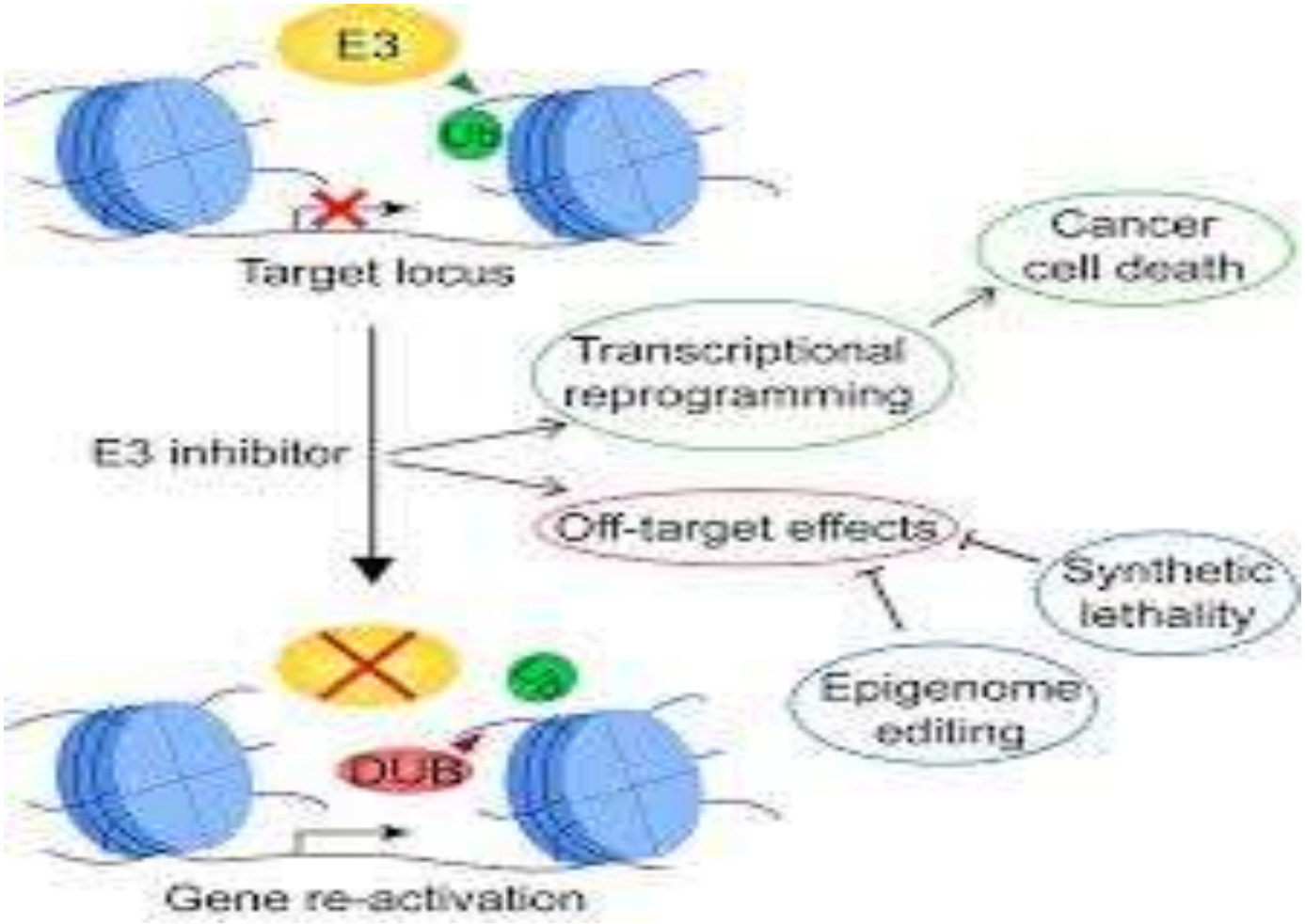
- Phosphorylation of histones, in particular phosphorylation of H2AX, has a role in DNA damage response and DNA repair.

- Rapid phosphorylation of **H2AX, at serine 129 (H2AX)** by the **PI3K kinases** at double strand break (DSB) sites, is one of the first and most easily detectable DNA damage signaling post-translational events.

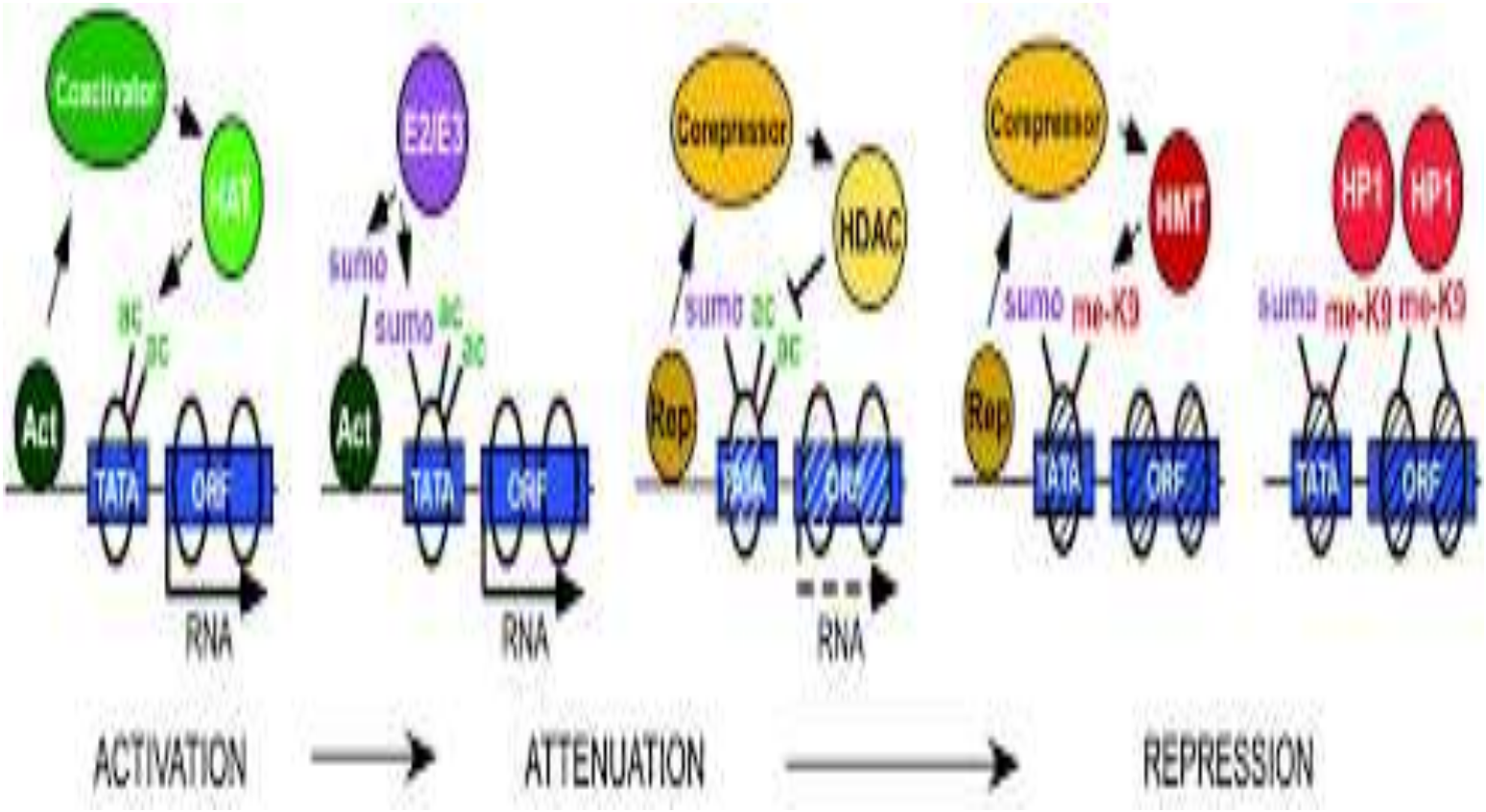


Dorine Rossetto, et. al., Epigenetics 7:10 2012

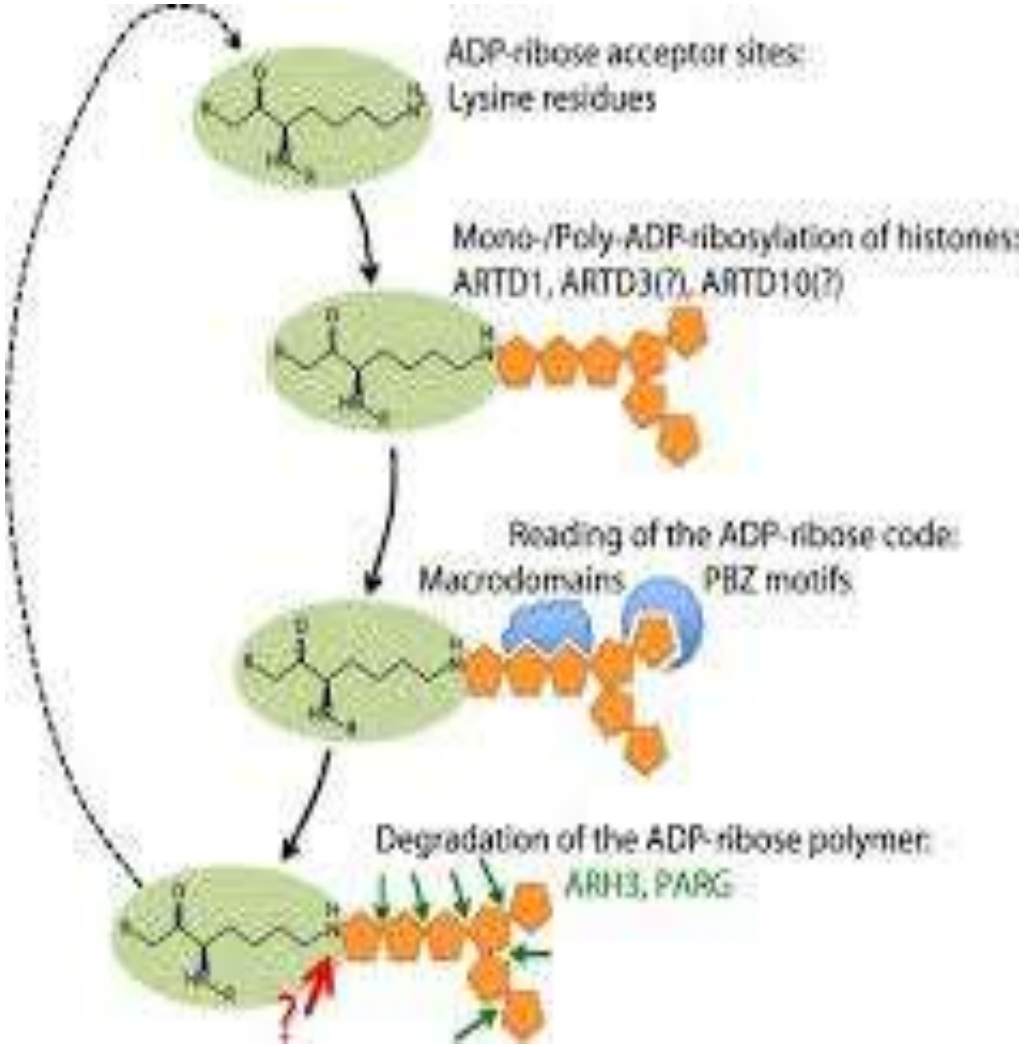
Histone ubiquitination

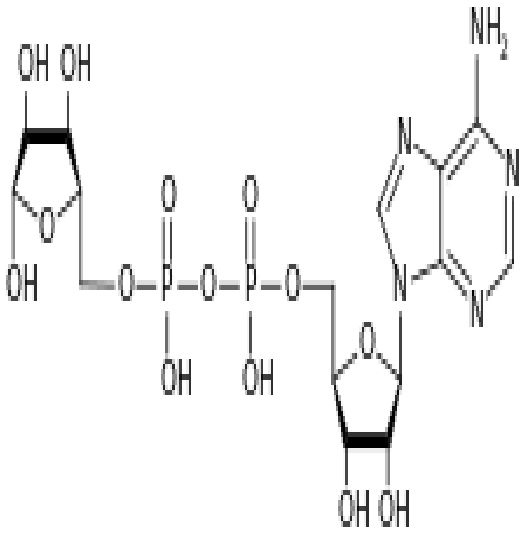


Histone Sumoylation



ADP Ribosylation

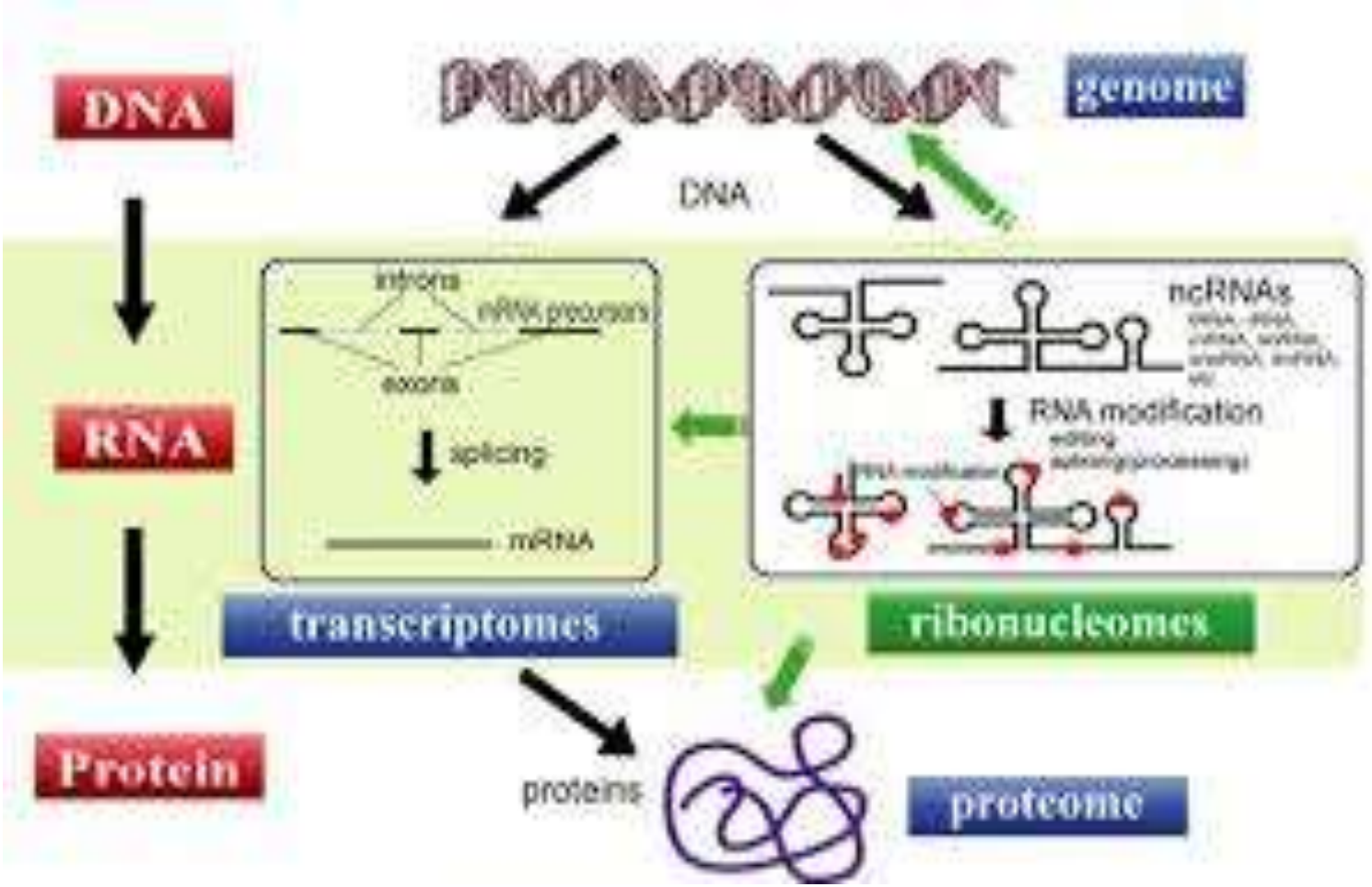




Histone Variants

- Variants of histone H3 - H3.1, H3.2, H3.3, TS H3.4
- Variants of histone H4 - H4.V
- Variants of histone H2A - H2A.X, H2A.Z, H2A.B, H2A.W
- Variants of histone H2B - H2B.1.

Non coding RNA in Epigenetics regulation



MiRNA – SS RNA, degrades mRNA

SiRNA – DS RNA, same as MiRNA additionally degrade viral RNA. Used as RNAi in research

SnRNA – regulate post transcriptional modification (splicing) of mRNA, also regulate transcription factors

LncRNA – involved in regulation of heterochromatin and euchormatin formation