

Histone

Histones are a group of proteins, that support the structure of chromatin by binding DNA in the nuclei of eukaryotic cells. They are positively charged, basic, as they contain a large amount of basic amino acids (such as arginine and lysine). There are strong ionic interactions between the positively charged histones and negatively charged DNA strands (phosphate groups).

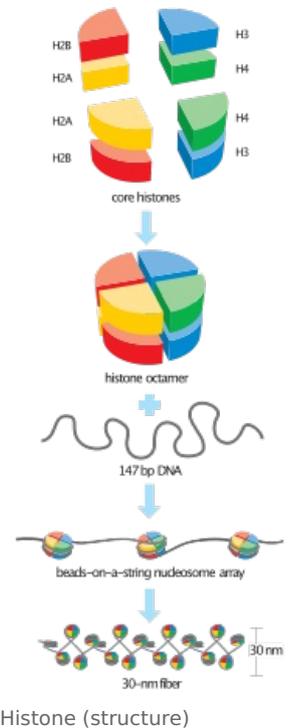
We can distinguish 5 subtypes of histones by **electrophoresis** (see the table below):

Overview of histone subtypes			
Histone	Lysine/Arginine Ratio	Number of amino acids	Molecular weight
H1	20.0	215	21 000
H2A	1.2	129	14 500
H2B	2.5	125	13 800
H3	0.72	135	15 300
H4	0.79	102	11 300

Histones are synthesised during the S phase of the cell cycle within the cell itself and are then transported to the nucleus.

H2A, H2B, H3 and H4 are the **core histones**, while H1 is the linker which is not a part of the histone octamer. Histones interact with the DNA strands in the form of an octamer (meaning it consists of 8 parts) - 2 molecules of each core histone form the **8-protein complex core (histone octamer)** around which DNA is wound. Together with the wound DNA, the histone octamers form a nucleosome with the diameter of **10 nm**. **Nucleosomes** are both a structural and functional complex of DNA (cca 150 base pairs) and a histone octamer - this gives the chromatin a "beads on a string" appearance under an electron microscope.

Linker histone H1 is not a part of the octamer and is connected to outer part of the nucleosome. Each nucleosome is associated exactly with one H1 histone, though its precise structure is not yet known. Its function is further stabilisation of the chromatic fibre and aid in formation of a higher complex of nucleosome array - **solenoid**. **Solenoid** is formed by **8-10 nucleosomes** - essentially, it is a chromatin fibre of a higher caliber (**30 nm in diameter**). The biggest human chromosome contains around 3000 solenoids.



Regulation of gene expression

The role of histone octamers is to control gene expression by reversible modifications of histones, which translate into changes in the structure of the chromosomes they are associated with. The histone modifications are reversible, post-translational - examples include mainly acetylation, methylation, but also phosphorylation, ubiquitinylation, etc.

Histone methylation

Histone methylation generally leads to **tighter DNA coiling, which decreases DNA transcription**. In certain cases however, methylation can also promote transcription - the final effect depends on the location and the number of methylated histones. The reaction is catalyzed by the enzyme *histone methyltransferase*, which targets mainly lysine and arginine.

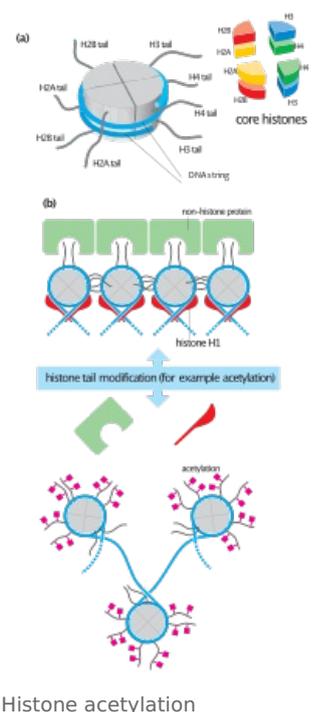
Histone acetylation

Histone acetylation decreases the positive charge of histone proteins (they become more negative), which leads to relaxation of the coiled DNA and thus increased gene transcription. Acetylation occurs mostly on positive lysine residues. Similarly to methylation, histone **deacetylation** causes DNA coiling and suppressed transcription.

Dysregulated acetylation may play a role in the pathogenesis of Huntington disease.

Euchromatin - active DNA is less condensed, which allows for gene transcription.

Heterochromatin - DNA cannot be transcribed as it is highly condensed, histones are highly methylated and deacetylated and chromosomes form structures of a higher caliber than solenoids.



That said, the primary structure of histones has been evolutionarily well-conserved. To give an example, the difference in the sequence of amino acids in the H4 histone of a broad bean and the analogous histone in cattle (more specifically beef thymus gland) is only 2 conservative amino acid exchanges - Ile instead of Val at the 60 position, and Arg instead of Lys at the 77 position. This serves as a proof that the structural effect of histones is greater than its regulatory role in gene expression (as mentioned above).

References

Related articles

- DNA Structure & Function
- Nucleosome
- Gene transcription

Bibliography

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