Acetylation and Methylation of Histones

Acetylation of histones is obviously an important method in the control of gene transcription. A recent study by Choudhary et al investigated the effect and prevalence of lysine acetylation in a range of other cellular pathways. The study discovered over 3600 acetylation sites on 1750 different proteins comprising the acetylome using high resolution mass spectrometry. These regulate a wide variety of dissimilar cellular function and showed acetylation as a prevalent form of post translational modification falling in terms of its frequency between the phosphoproteome and the spectrum of ubiquitinated proteins. It is a highly conserved process occurring in many different cellular lines from prokaryotes to human beings, and being as prevalent as phosphoproteins found in the evolutionary tree. The authors found that compared to phosphorylation sites in proteins, which are found in more disordered regions, acetylation sites are found in more structured regions with significant secondary structure.

Acetylation eliminates the positive charge on lysine side chains in a reversible process. It has already been established that acetylation of lysine side chains was a key component of DNA damage repair as it modifies histone protein tails found in the DNA. However, recently it has been shown that acetylation's effects extend to regulation of other cellular functions. Most commonly acetylation plays a role in nearly all nuclear functions, but it also plays a surprisingly big role in cytoplasmic functions. One of the new cellular functions investigated was the involvement of acetylation in regulating macromolecular complexes within the cell pertaining to functions such as signal transduction, DNA damage repair, and the cell cycle. One example protein included in the study is the 14-3-3 protein which binds specifically to phosphoserine or phosphothreonine in phosphorylated peptides. Four different lysines in the protein were mutated to glutamine in an attempt to determine the effect of acetylation on the protein's binding. Acetylation was found to regulate binding as the enzyme's activity was severely harmed by mutation. This has been seen in other cellular processes where acetylation has lead to regulation of enzymatic activity. In addition, the study discovered that there is important interaction between phosphorylation and acetylation. This interaction or cross talk between acetylation and other post translational modification methods in regulating cellular activity has been observed in the protein p53 as well which plays an important role in repairing damaged DNA. Acetylation data can be found at Phosida.
The language metaphors of transcription (decoding one nucleic acid - DNA - into another - RNA) and translation (decoding a nucleic acid written in the language of ribonucleotides into a protein written in the language of amino acids) can be extended to epigenetic modifications histones proteins in nucleosomes to produce the "histone code":

- writers: enzymes like histone acetyltransferases and methyltransferases the modify histones (on Lys and Arg side chains), especially on tails extending from the nucleosome;
- erasers: enzymes like histone deacetylases and lysine demethylases
- readers: proteins that recognize and bind to post-translationally modified histones including bromodomain-containing proteins (which recognize methylated Lys side chains), and methyl-Lys and methyl-Arg binding domain proteins

These protein are increasingly becoming targets for drug design as a way to alter gene transcription.

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