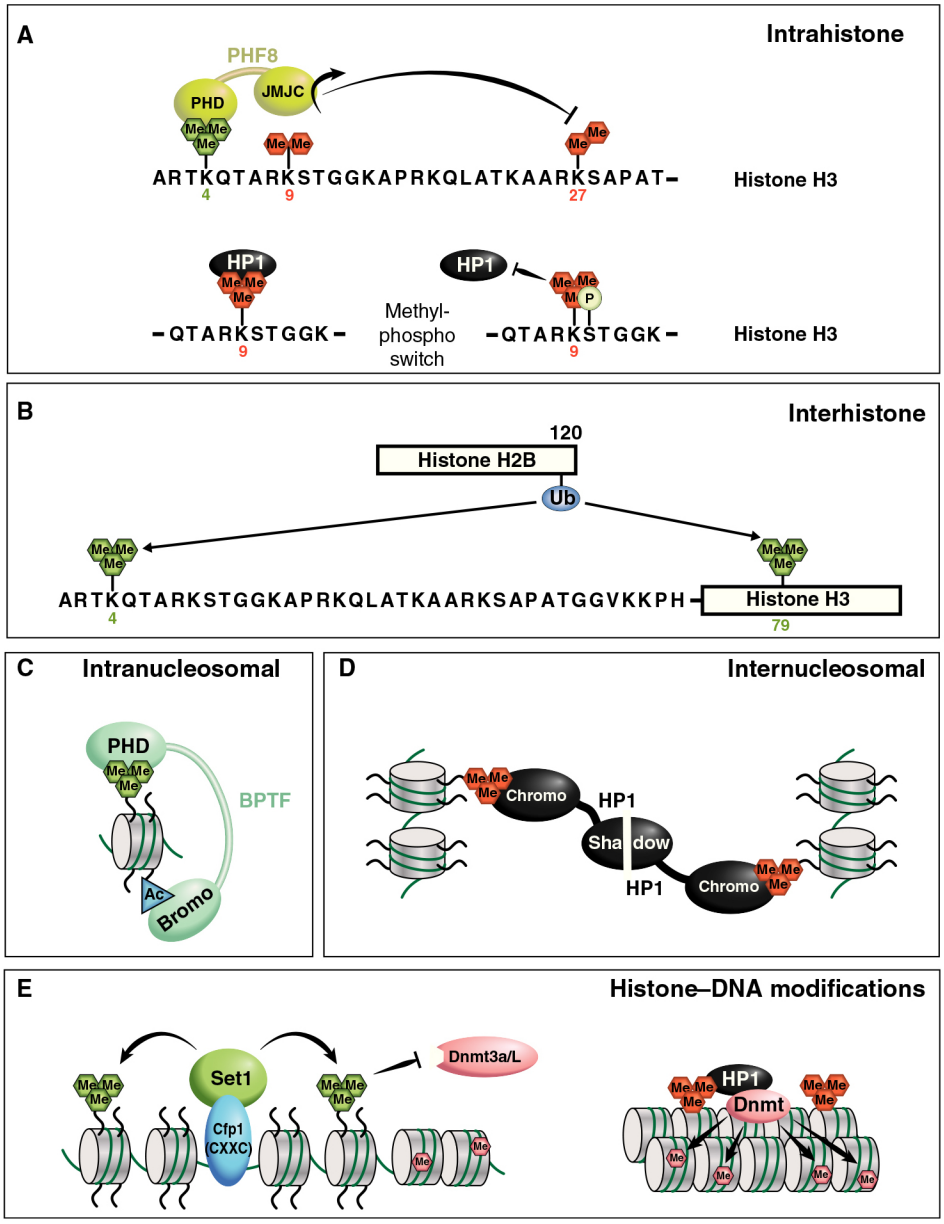

Figure 12. Combinatorial readout of chromatin modifications. (*A*) Intrahistone interplay: Histone modifications within one histone tail generate a specific downstream readout. For example, the position of the catalytic JMJC domain of the PHF8 KDM is structurally constrained to remove only H3K9me2, but not H3K27me2 because of its anchoring to chromatin via H3K4me3 binding to its PHD domain. The KIAA1718 KDM operates via a similar PHD domain-anchoring mechanism to H3K4me3, but because of different protein structure only acts on H3K27 and not H3K9 methyl marks. Another illustration is the ejection of HP1 bound to H3K9me3 when the neighboring H3S10 becomes phosphorylated, a mechanism known as "phospho-methyl" switch. (*B*) Interhistone cross talk: Modifications on two distinct histones influence each other. For example, H2BK120ub is a prerequisite for H3K4me3 and K3K79me3 to occur. (*C*) Intranucleosomal association: A chromatin reader is recruited via two distinct modifications within one nucleosome. For example, the PHD domain and bromodomain of BPTF (bromodomain and PHD finger transcription factor) bind to H3K4me3 and H4K16ac within one nucleosome. (*D*) Internucleosomal association: A chromatin reader interacts with histone modifications present on different nucleosomes. For example, the two chromodomains of HP1 dimers link H3K9me3-containing nucleosomes. (*E*) Histone-DNA modification cross talk: Modifications on histones and DNA influence each other. For example, recruitment of the Set1 KMT via Cfp1 bound to unmodified CpG-rich DNA results in H3K4me3 chromatin, which, in turn, inhibits association of Dnmt3a/L, thereby protecting these regions from DNA methylation. Conversely, recruitment of Dnmts to H3K9me3 chromatin via HP1 leads, subsequently, to DNA methylation.