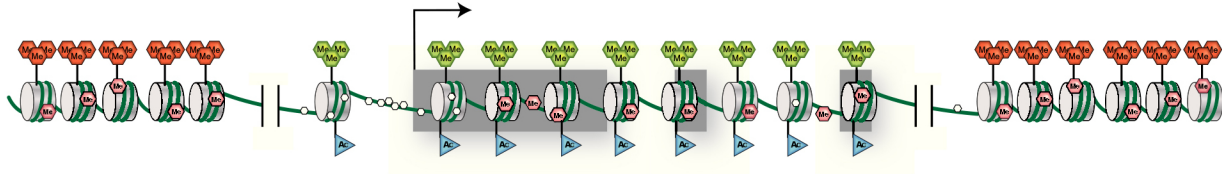


A Normal epigenome



B Cancer epigenome

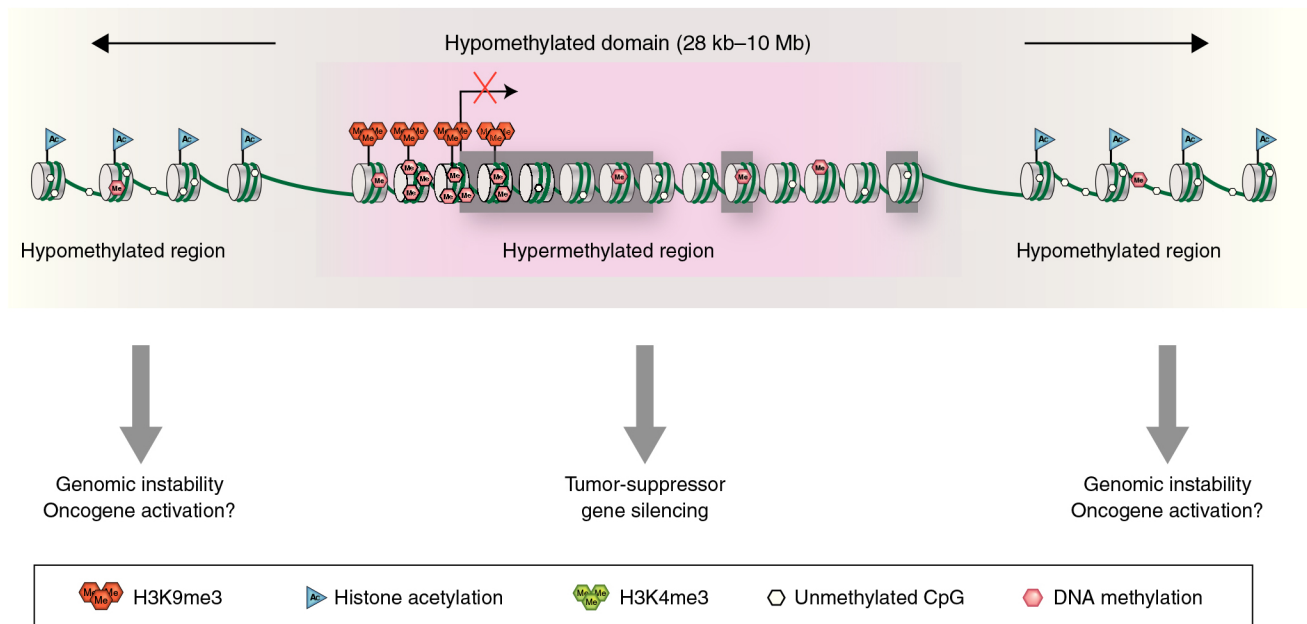


Figure 4. Chromatin structural changes in cancer cells. (A) In a typical cell, a CpG-island-containing active gene can be recognized by virtue of a nucleosome-depleted promoter, absence of promoter DNA methylation, but marked by H3K4me3 surrounding the promoter and histone acetylation along the locus. Gene body CpG methylation often can be observed. Nongenic regions flanking an active gene are frequently marked by repressive epigenetic marks, such as H3K9me3 and 5mC. (B) The cancer epigenome is characterized by simultaneous global losses in DNA methylation (gray shading), interspersed with silenced genes that have abnormal gains of DNA methylation and repressive histone modifications in CpG island promoter regions. These silenced genes may be hypomethylated in their gene body, similar to surrounding chromatin. The hypomethylated regions can have an abnormally open nucleosome configuration and acetylated histone lysines. Conversely, abnormal DNA hypermethylation in promoter CpG islands of silenced genes is associated with nucleosomes positioned over the transcription start sites.