



**Figure 33.** Epigenetic therapy. (A) The epigenome of a cell reflects cellular identity and differentiation state. Compared with differentiated cells, stem cells and proneoplastic cells are characterized by more open chromatin (high histone acetylation), whereas senescent and nonproliferative cells develop large heterochromatic foci (high histone and DNA methylation). The goal of epigenetic therapy is to reset the perturbed epigenomic profiles of tumor cells by the use of small chemical inhibitors of epigenetic enzymes (e.g., HDACi, KMTi, DNMTi). (B) In addition to chromatin-modifying enzymes, chromatin readers can also be targeted by epigenetic therapy. For example, BET (bromodomain and extraterminal) inhibitors (BETi) specifically block the binding of the BRD3/4 bromodomains to promoter-proximal histone acetylation marks, thereby preventing transcriptional elongation of key target genes (MYC, E2F, and NF- $\kappa$ B).