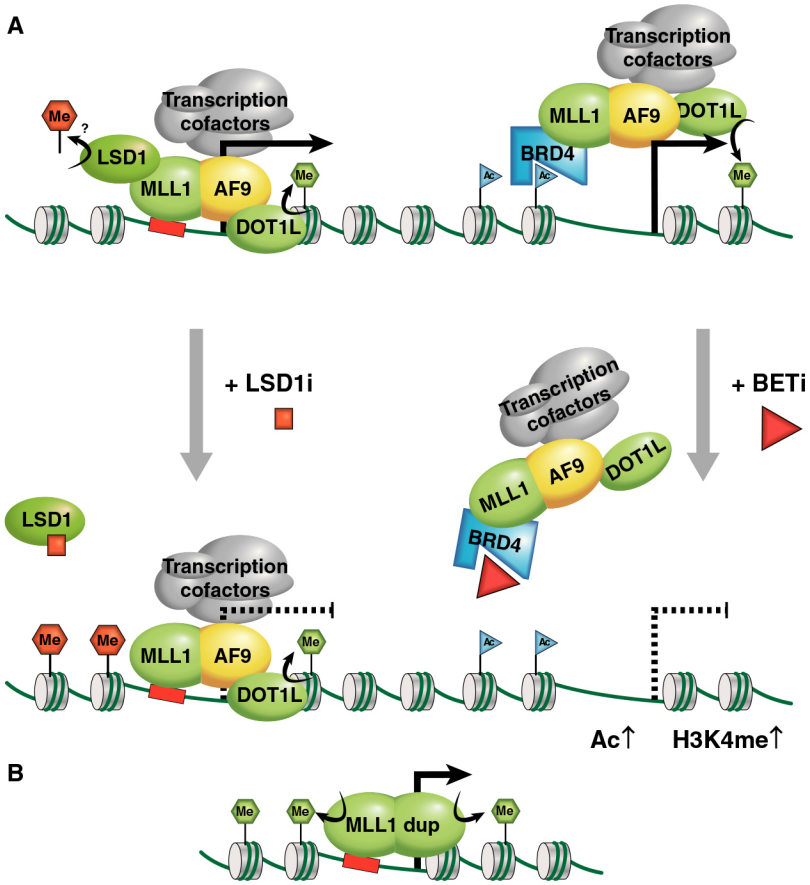

Figure 2. MLL as an oncogene. (*A*) The MLL1-AF9 (or ENL) fusion oncoprotein activates transcription via two possible mechanisms; the *left* mechanism attributes recruitment of MLL1-AF9 to chromatin via the MLL1 portion, and transcription is activated via association with cofactors, including the DOT1 methyltransferase, methylating H3K79 (green hexagon) and the pTEFb complex, which modifies RNA Polymerase II into the active elongating form. (*B*) The partial duplication of an MLL gene can result in duplication of an internal region that includes chromatin binding features and protein–protein interaction domains, providing oncogenic methyltransferase H3K4me3 activity and increased transcriptional activation. LSD1 may be involved via the MLL supercomplex, or a transcription elongation complex contributing to oncogenic activity through H4K4me2 or H3K9me2 demethylase activity. LSD1 inhibition somehow reduces the oncogenic program, promoting differentiation. In the mechanism on the *right*, recruitment of MLL1-AF9 to chromatin is attributed to its association with BRD-2, -3, or -4 via acetylated chromatin. This mechanism of gene activation can therapeutically be targeted via treatment with BET inhibitors.