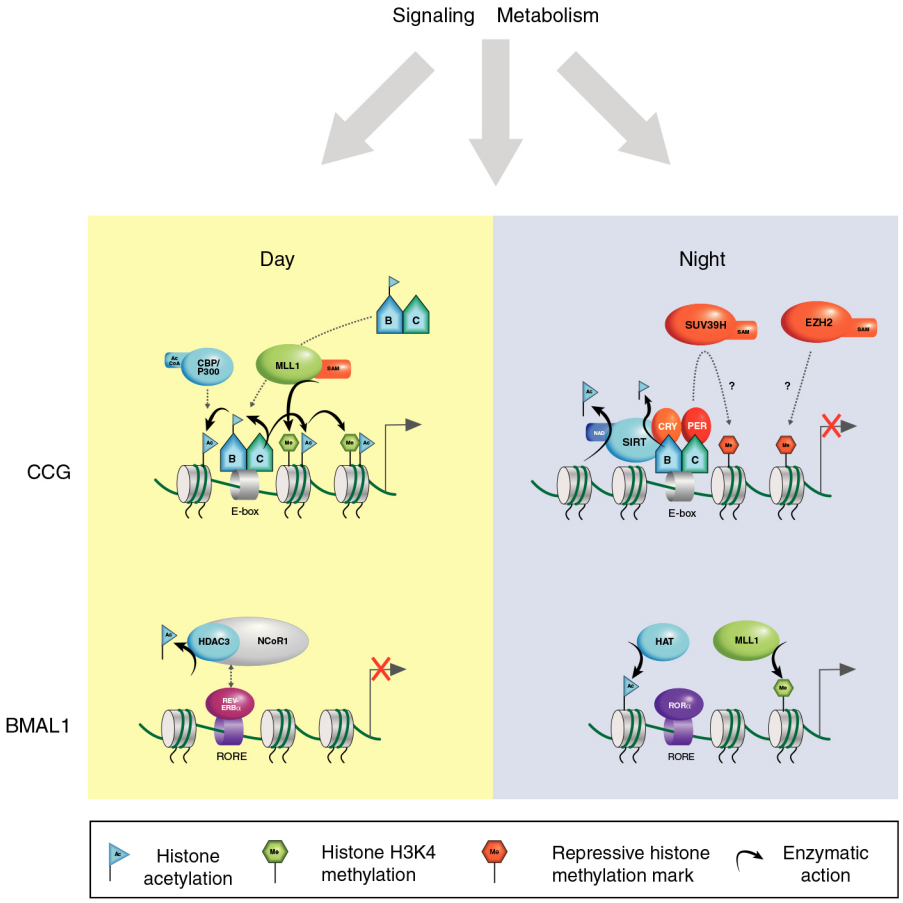

Figure 6. Key chromatin-remodeling factors involved in the activation and repression of CCGs and BMAL1. Recruitment of the CLOCK:BMAL1 heterodimer to CCGs during the day is facilitated by binding to the E-box and via the MLL1 enzyme. A transcriptionally active chromatin conformation is achieved through the combined action of H3K4me3, via the MLL1 lysine methyltransferase enzyme, and the histone acetylating activity of CLOCK, CBP, and P300 (cyan shaded proteins). Repressive chromatin conformations at CCGs may be achieved by the SIRT1-mediated deacetylation of histones at H3K9, K14, and H4K16, and possibly the actions of EZH2-catalyzed H3K27me3 or SUV39H-catalyzed H3K9 methylation. SIRT1 also has an inhibitory effect by deacetylating BMAL1 K537-ac. Silencing of RORE-containing genes, such as BMAL1, by day is, in part, achieved by recruitment to the RORE-bound inhibitor, REV-ERBα, of the NCoR1 complex and associated HDAC3 deacetylase. At night, predominance of RORα-bound ROREs promotes active chromatin structure, typified by histone acetylation and H3K4 methylation.