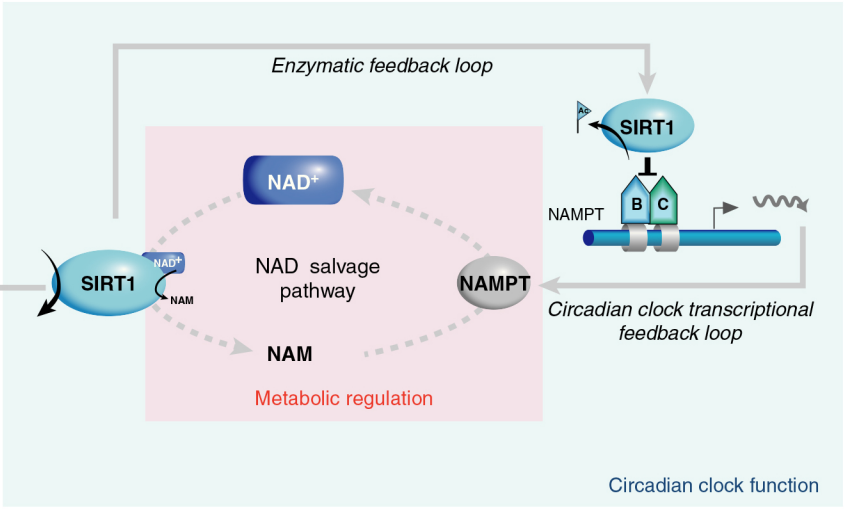

Figure 7. Linking the circadian clock with the NAD^+ salvage pathway. The NAMPTenzyme is the limiting factor in the NAD^+ salvage pathway; thus, because the NAMPT gene is regulated by the circadian CLOCK:BMAL1 machinery, its product, the NAD^+ metabolite, oscillates via this NAMPT transcriptional feedback loop. The HDAC, SIRT1, among other functions, acts as a repressor of the clock machinery by effecting deacetylation of the BMAL1 protein and histones at CCGs (see also Fig. 6). Thus, whereas the enzymatic activity of SIRT1 oscillates in a circadian manner via the circadian controlled supply of its metabolite, NAD^+, its activity also constitutes an enzymatic feedback loop for the circadian clock via its repressive activity at the NAMPT gene.