



**Figure 4.** Cell-cycle regulation of centromere heterochromatin assembly. (A) Heterochromatin located at chromosomal centromeres becomes differentially methylated and phosphorylated on histones throughout the cell cycle as indicated. These modifications control the binding of the heterochromatin protein Swi6. During mitosis Swi6 is displaced by H3S10 phosphorylation. Swi6 binding is reestablished during subsequent DNA replication (S phase) when a more accessible chromatin structure permits RNA Pol II to transcribe centromeric DNA. This, in turn, recruits the RNAi machinery to direct H3K9me methylation. (B) Replication-coupled RNAi model (Li et al. 2011). This figure illustrates an alternative model for how RNAi works at centromeres. Here, RNAi serves to release RNA Pol II from chromatin to avoid collision with DNA replication machinery during S phase. See text for further details. (A, Adapted from Djupedal and Ekwall 2008.)