

Figure 10. The order of events in differentiating XX ES cells. The diagram summarizes the order in which different silencing pathways are integrated during establishment of X inactivation in differentiating XX ES cells. Early events, depletion of RNA Pol II, loss of H3K4me3/H3K9Ac, and deposition of Polycomb-associated modifications occur coincident with the onset of *Xist* RNA expression. H4 hypoacetylation and a transition to late replication in S-phase occur slightly later. Enrichment for macroH2A, Smchd1 Ash2l, and hnRNPU/SAF-A occur in a defined temporal window relatively late in the differentiation time course. Accumulation of DNA methylation over CpG island occurs slowly following recruitment of Smchd1, although a subset of CpG islands acquire DNA methylation more rapidly and in a Smchd1-independent manner.

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