Set3 is one of two proteins in yeast that, like Drosophila Trithorax, contains both SET and PHD domains. Set3p forms a complex called Set3C with Snt1p, Sif2p, cyclophilin Cpr1p, Hos2p, Hos4p, and Hst1p, that includes both NAD-dependent and NAD-independent histone deacetylase activities. Set3C represses early/middle sporulation genes, including those encoding key meiotic regulators such as the IME2 protein kinase and the NDT80 transcription factor. Hst1p is also present in a complex with transcriptional repressor Sum1p. However, Hst1p is not required for meiotic repression by Set3C, suggesting that Set3Cand not Hst1p-Sum1p, is the meiotic-specific repressor of early/middle sporulation genes. Homology searches suggest that Set3C is the yeast analog of the mammalian HDAC3/SMRT complex.