



Figure 1. Structural features of SUV39H1 and SUV39H2. (A) Ribbon diagram of amino-terminal chromodomain of SUV39H1 (PDB 3MTS). (B) Carboxyl-terminal SET domain structure of SUV39H2 (PDB 2R3A). (C) Formation of the pseudoknot by motifs III and IV. (D) Formation of the active site showing the methyl donor (*S*-adenosyl-L-methionine [AdoMet]), target H3K9 lysine, catalytic Y280 residue, and F370 Phe/Tyr Switch (Collins et al. 2005). AdoMet-dependent methyltransferases (including HKMTs) share a reaction mechanism in which the nucleophile acceptor (NH₂) attacks the electrophilic carbon of AdoMet in an S_N2 displacement reaction. (E) SUV39H1 and H2 have a pre-SET segment containing nine invariant cysteines, the SET region containing four signature motifs, and the post-SET region containing three invariant cysteines. An enlargement of the pre-SET Zn₃Cys₉ triangular zinc cluster structure is illustrated on the *bottom left* and the post-SET zinc center on the *bottom right* panel.