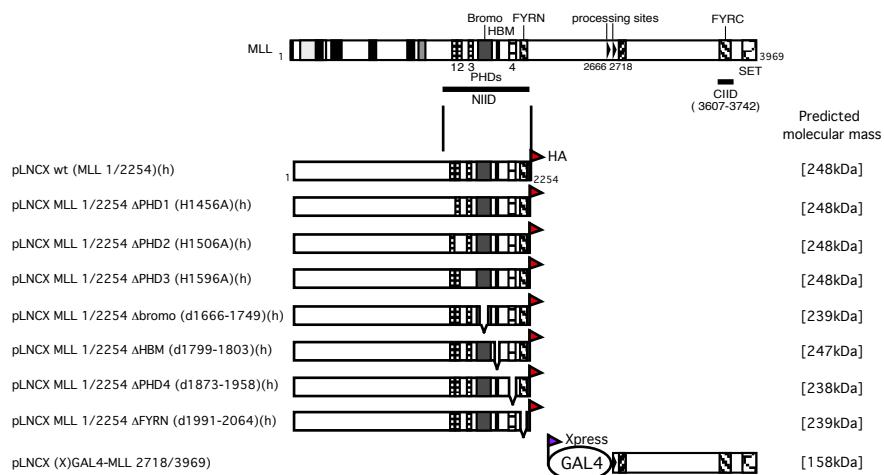


Figure S1

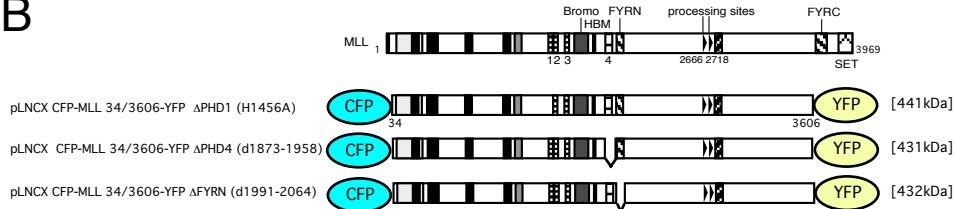
Graphical representations of various constructs used in the manuscript.

MLL mutant proteins are shown schematically and grouped according to the experiments in which they were employed and the relevant figure numbers in the main text: (A) proteins shown in Fig. 4A and B, (B) Fig. 4C, (C) Fig. 4E and F, (D) Fig. 5B, (E) Fig. 5C, (F) Fig. 5D, (G) Fig. 6A, (H) Fig. 6B, (I) Fig. 6C, (J) Fig. 6D, (K) Fig. 6E, and (L) Fig. 6F. Predicted molecular mass (kDa) of each mutant is shown on the right.

A



B



C

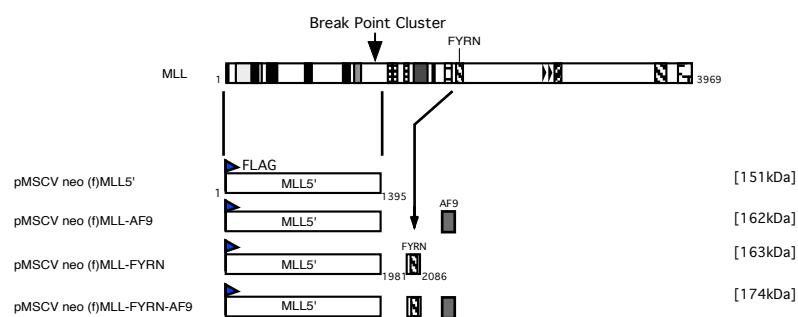


Figure S1 continued

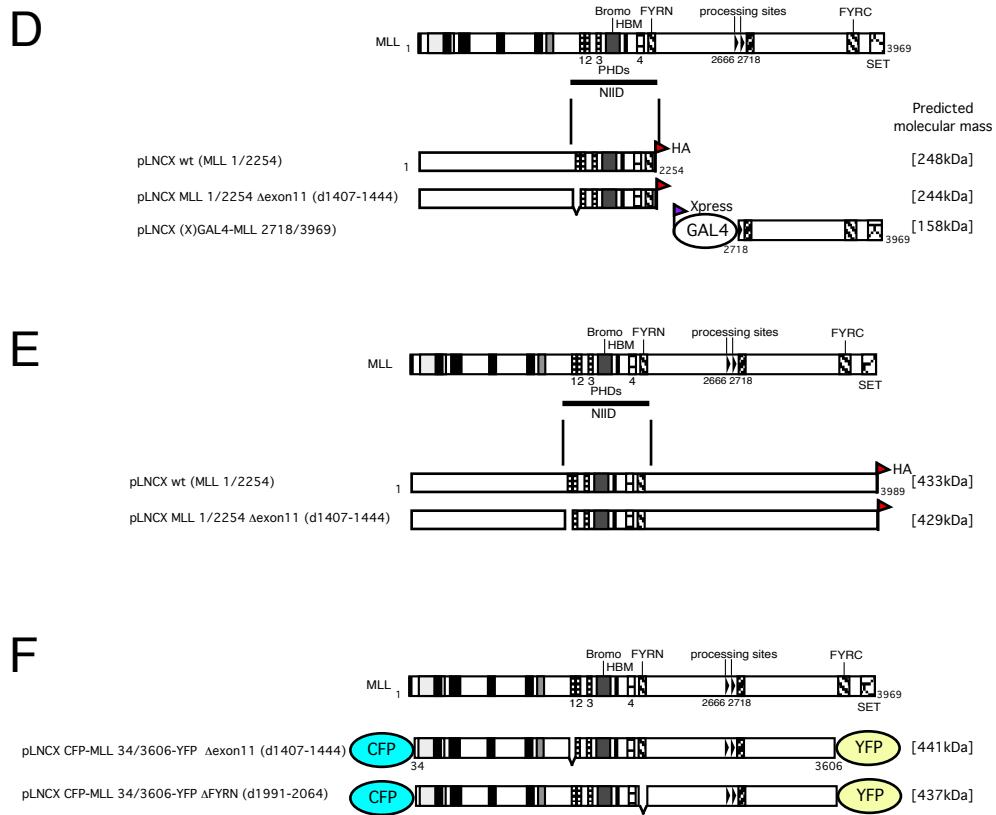
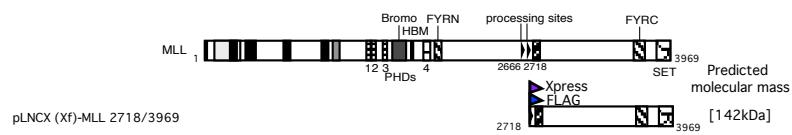
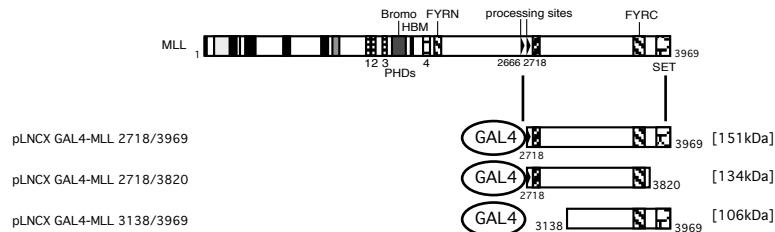


Figure S1 continued

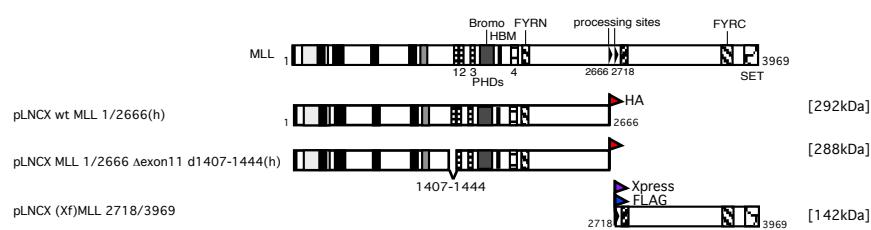
G



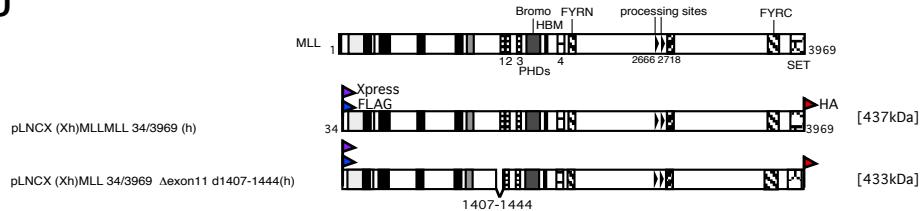
H



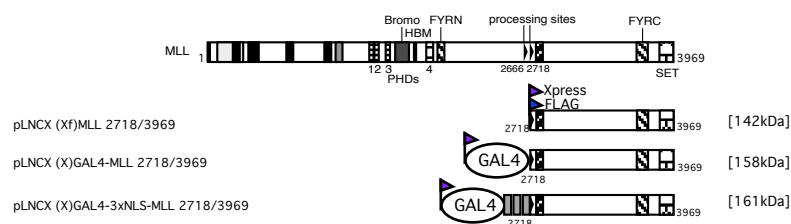
I



J



K



L

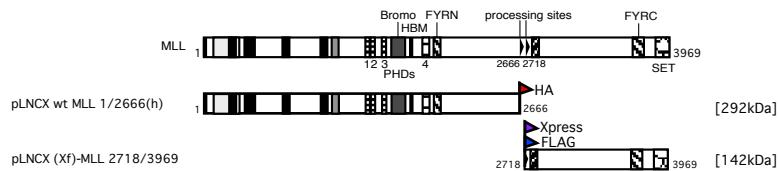


Figure S2

MLL mutants that do not associate with MLL^C can interact with HCF-1.

A. Schematic representation of the mutants. Predicted molecular mass of each mutant is shown on the right.

B. IP-western blot analysis was performed for various MLL 1/2254 mutants that do not associate with MLL^C. MLL 1/2254 mutants were transiently expressed in 293T cells. The cell extracts were subjected to immunoprecipitation (IP) with anti-HA (3F10) antibody followed by immunoblotting. The precipitates and input samples indicated on the top were immunoblotted with anti-HA (top panel) or anti-HCF-1C (H12) (bottom panel) antibodies.

C. IP-western blot analysis was performed for MLL1/2254 Δexon11 mutant as in panel B. HCF-1 binding was observed for the Δexon11 mutant.

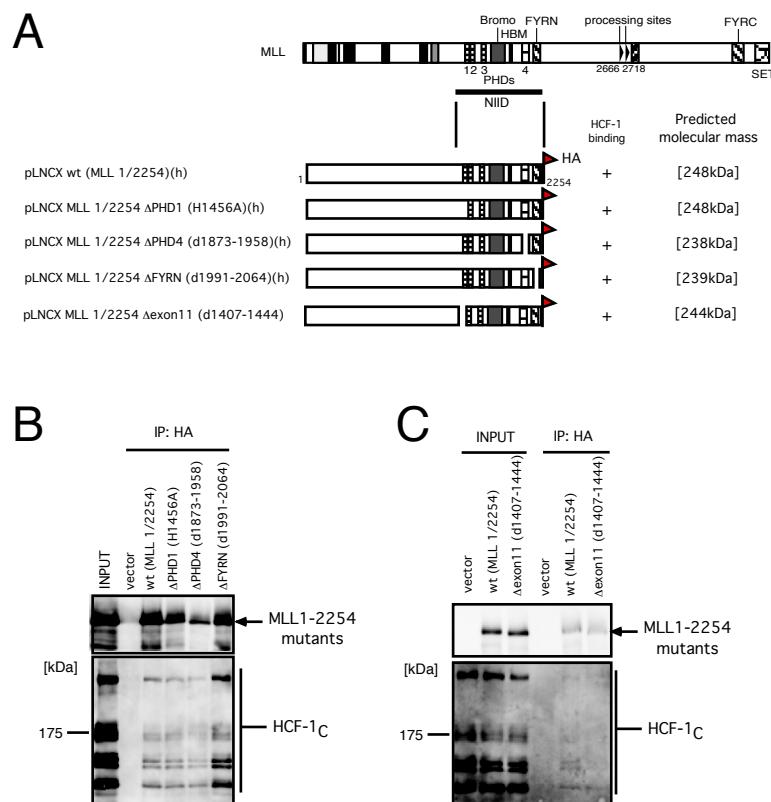


Figure S3

The FYRN domain is required for holocomplex formation and destabilization in various contexts.

A. Schematic representation of the full-length MLL mutants. Binding property with MLL^C , susceptibility to destabilization, and predicted molecular mass of each mutant are shown on the right.

B. IP-western blot analysis was performed for various MLL full-length mutants tagged with an HA epitope at the C-terminus. MLL mutants were transiently expressed in 293T cells. The cell extracts were subjected to IP with anti-MLLN antibody (mmN4) followed by immunoblotting. The precipitates and input samples indicated on the top were immunoblotted with anti-MLLN (mmN4) (top panel) or anti-HA (3F10) (bottom panel) antibodies.

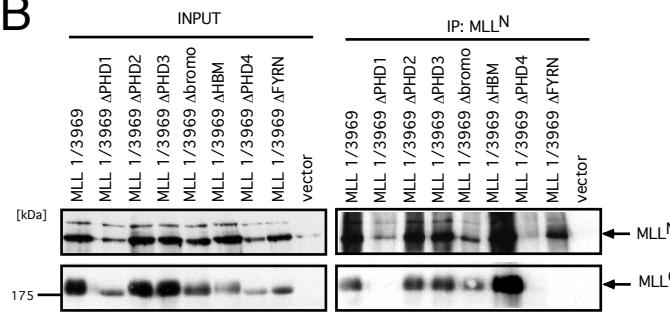
C. Schematic representation of the various MLL deletion mutants. Binding property with MLL^C , susceptibility to destabilization, and predicted molecular mass of each mutant are shown on the right.

D. IP-western blot analysis was performed for various MLL deletion mutants as in Figure 4B. MLL deletion mutants were co-expressed with Xpress-tagged GAL4- MLL^C [(X) GAL4- MLL^C] in 293T cells. The cell extracts were subjected to IP with anti-MLLN (mmN4) antibody, and the precipitates and input samples indicated at the top were immunoblotted with anti-MLLN (mmN4) (top panel) or anti-Xpress (middle bottom two panels) antibodies.

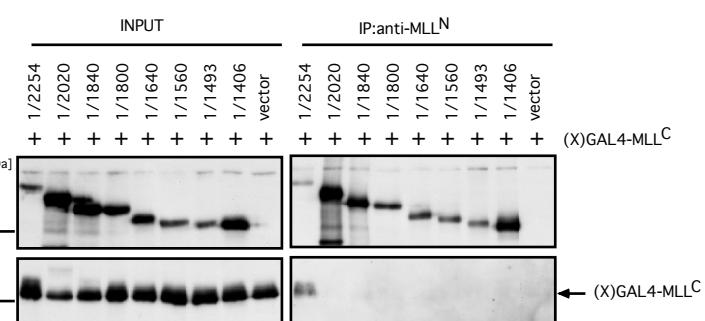
A



B



D



C

