

Essential role of lncRNA binding for WDR5 maintenance of active chromatin and embryonic stem cell pluripotency.

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Public Summary:

The WDR5 subunit of the MLL complex enforces active chromatin and can bind RNA; the relationship between these two activities is unclear. Here we identify a RNA binding pocket on WDR5, and discover a WDR5 mutant (F266A) that selectively abrogates RNA binding without affecting MLL complex assembly or catalytic activity. Complementation in ESCs shows that WDR5 F266A mutant is unable to accumulate on chromatin, and is defective in gene activation, maintenance of histone H3 lysine 4 trimethylation, and ESC self renewal. We identify a family of ESC messenger and lncRNAs that interact with wild type WDR5 but not F266A mutant, including several lncRNAs known to be important for ESC gene expression. These results suggest that specific RNAs are integral inputs into the WDR5-MLL complex for maintenance of the active chromatin state and embryonic stem cell fates

Scientific Abstract:

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