

Genome-Wide Isoform Specific KDM5A/JARID1A/RBP2 Location Analysis Reveals Contribution of Chromatin-Interacting PHD Domain in Protein Recruitment to Binding Sites

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Abstract : RBP2 has shown to be important for cell differentiation control through epigenetic mechanism. The main aim of the present study is genome-wide location analysis of human RBP2 isoforms that differ in a histone-binding domain by ChIPseq. It is conceivable that the larger isoform (LI) of RBP2, which contains a specific H3K4me3 interacting domain, differs from the smaller isoform (SI) in genomic location, may account for the observed diversity in RBP2 function. To distinguish the two RBP2 isoforms, we used the fact that the SI lacks the C-terminal PHD domain and hence used the antibodies detecting both RBP2 isoforms (AI) through a common central domain, and the antibodies detecting only LI but not SI, through a C-terminal PHD domain. Overall our analysis suggests that RBP2 occupies about 77 nucleotides and binds GC rich motifs of active genes, does not bind to centromere, telomere, or enhancer regions, and binding sites are conserved compare to random. A striking difference between the only-SI and only-LI is that a large number of only-SI peaks are located in CpG islands and close to TSS compared to only-LI peaks. Enrichment analysis of the related genes indicates that several oncogenic pathways and metabolic pathways/processes are significantly enriched among only-SI/AI targets, but not LI/only-LI peak's targets.

Keywords : bioinformatics, cancer, ChIP-seq, KDM5A

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