

Functional annotation of lncRNAs involved in epigenetic regulation

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Many long non-coding RNAs have been experimentally associated with chromatin. Yet, for the majority of chromatin-bound lncRNAs, the regulatory mechanism remains unclear. We developed a computational pipeline to identify lncRNAs that could affect DNA methylation, histone modifications, and, consequently, gene expression. Briefly, the pipeline consists of three major steps: (1) correlation analysis between a lncRNA expression and a presence of an epigenetic mark in a specific genomic location; (2) functional analysis of gene expression change in response to a lncRNA knockdown; (3) colocalization analysis of a lncRNA and target genomic region. We applied the pipeline to ten histone modifications and DNA methylation profiles in multiple cell types available from ENCODE, for functional analysis we used NNN lncRNA knockdown experiments from FANTOM6 Pilot. We detected several dozens of lncRNAs potentially involved in writing or erasing a specific histone modification, as well as putative genomic regions where the respective modifications are regulated by particular lncRNAs, both previously reported and unknown.

For several detected lncRNA-histone modification pairs we performed ChIP-seq analysis in the knockdown system to validate the link. At least three lncRNAs are extremely promising candidates for histone modification regulators.