Abstract

The phenomenon, where transcription of an induced gene propagates to its neighbouring genes is known as transcriptional ripple. A study by Ebisuya et al. demonstrated that addition of fibroblast growth factor in quiescent mouse NIH3T3 cells; rapidly induce immediate-early genes (IEGs) and this induction of target genes is accompanied by up -regulation of their neighboring genes. This suggests that transcriptional activation has a ripple-like effect. However, epigenetic basis and the functional significance of transcriptional ripple effect are not yet understood. Here, we have investigated the transcriptional ripple effect in Estrogen induced transcription in MCF-7 breast cancer cell line. We identified 151 estrogen-receptor(ER) target and their neighbouring genes; out of which 89 neighbouring genes showed significant transcriptional up/down regulation upon estrogen induction. Further, we comprehensively analyzed different genomic, epigenomic and functional attributes of estrogen-receptor target and their nearest neighboring genes. We had following key observations: 1) Affected neighbouring genes were more distant from the target genes as compared to unaffected genes, significance of which is not entirely clear. 2) Regions having affected and unaffected neighbouring gene did not differ in their gene density. 3) Chromatin state analyses through ChromHMM platform, suggested that the affected neighboring genes more likely to have „active promoter" as compared to unaffected genes. 4) Most affected neighboring genes had „High CpG" promoters as compared to ER-target genes and the unaffected neighboring genes. 5) Analyses of RNAPII ChIA-PET data revealed no significant association with the long range chromatin interaction between target and neighboring genes. Overall, our observations suggest that the induction of a gene can interfere with the process of active transcription in the neighborhood and that the chromatin state and the CpG content of the neighboring gene-promoter seemingly determines whether or not the gene would be perturbed. Further exploration of other genome-wide datasets would, hopefully, unravel the underlying functional significance of such observations.
Keywords Transcriptional ripple effect, chromatin states, Normalized CpG content, chromatin interaction.