

Analysis of long-range chromatin interaction and how transcription factors are involved to regulate gene expression

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DNA sequences in nucleus are highly condensed to form chromatins. Due to the compact three-dimensional conformation of chromatin, DNA sequences with large genomic distance are possible to be physically close. The spatial proximity between distant genomic regions is informative in explaining how distant cis-regulatory elements affect gene expression. With the advance of biological technologies we are able to detect the three-dimensional structure of chromosomes and long-range interaction of high resolution. Here we process human Hi-C data to draw a whole-genome interaction map with a resolution of 10kb. Next we explore how different transcription factors are involved in the long-range chromatin interaction. We define that one transcription factor mediates the interaction if it has peaks binding to both bins of an interacting pair and these peaks are enriched with Hi-C reads. We find the highly active transcription factors involved in long-range interaction are informative for the cellular function. In addition, from the colocalization of binding peaks of different transcription factors in long-range interaction sites we detect transcription factor complex. Finally, by the analysis on the enrichment of important biological marks in long-range interaction sites, including CAGE tags, histone modifications, DNA methylation and DHS sites, we find in different types of cell the most influential active regulatory marks participating in long-range interaction are differing from each other. In conclusion, we employ Hi-C data and multiple transcription factor binding profiles in different types of cell to study the role of transcription factors and histone modifications in long-range interaction and gene expression regulation.

Further evidence that the 3'Untranslated Region of the CHOP mRNA possesses mRNA destabilizing effect.

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The transcription regulatory factor known as Chop is commonly induced to express in stressed cells. In most cases, the expression of CHOP is associated with apoptosis. Although the regulation of CHOP expression at the transcriptional level has been studied to considerable details, the involvement of post-transcriptional mechanism such as mRNA stability has not been much addressed. We previously provided indirect evidence that the 3'UTR of CHOP mRNA had an mRNA destabilizing effect. The objective of this study was to provide more direct evidence to support this hypothesis. A reporter plasmid was constructed so as to express an EGFP mRNA that has its original 3'UTR replaced with CHOP-3'UTR (EGFP1-mRNA) upon transient transfection into HeLa cells. The expressed EGFP1-mRNA was extracted from the transfected cells, reverse transcribed to produce the cDNA, and quantified by real time PCR. Results demonstrated that the intracellular level of EGFP1-mRNA was significantly lowered than that of the control (unmodified EGFP mRNA). To see if the relatively lower steady state level of EGFP1-mRNA were due to decreased transcription of the reporter plasmid, or more rapid degradation of EGFP1-mRNA, the degradation rates of EGFP1-mRNA and its control mRNA were measured. The results showed that the rate of degradation of EGFP1-mRNA was higher when compared to the control, hence providing further support that the 3'UTR of CHOP mRNA had an intrinsic destabilizing mechanism to prevent inadvertent expression of the CHOP gene in unstressed cells. Further experiments are being performed to confirm such a hypothesis.