Z-DNA Formation and Transcriptional Activation in the Human Genome.

So-I Shin[1], Seokjin Ham[1], Jihwan Park[2], Seong Hye Seo[1], Chae Hyun Lim[2], Hyeongrin Jeon[1], Jounghyun Huh[1], Tae-Young Roh[1,2,*]

[1] Department of Life Sciences, [2] Division of Integrative Biosciences & Biotechnology, Pohang University of Science and Technology (POSTECH), Pohang, Republic of Korea

Abstract

In human cells, most double stranded DNA consists of B-DNA structure. But Z-DNA also exists as a form of left-handed double helical structure. Much of the experimental evidence has shown that Z-DNA in some specific genes plays a significant role in biological functions such as transcriptional regulation and genome stability. However, the biological meaning of Z-DNA was not fully explored due to the lack of precise map for Z-DNA forming sites (ZFSs) in human cells. To obtain the genome-wide map of ZFS, Zaa consisting of two Z-DNA-binding domains were used for ChIP-Seq analysis. A total of 391 ZFSs were found and their functions were examined in HeLa cells. Large portion of ZFSs was enriched in the promoter regions and mainly contain sequences with high potential to form Z-DNA. Z-DNA structure in vivo was found not only in the sequence context of alternating purine/pyrimidine but also in irregular Z-DNA forming sequences. The closest genes to ZFSs are were occupied by RNA polymerase II at their promoters and highly expressed. Furthermore, ZFSs were associated with epigenetic modifications such as H3K4me3 and H3K9ac which are active histone marks whereas ZFSs were not found in regions enriched for repressive histone marks. The correlation of ZFSs with active transcription was confirmed by reporter assay system. Overall, this study suggests that Z-DNA formation is affected by chromatin structure as well as sequence composition, and is involved in transcriptional activation. The genome-wide map of ZFSs in the human genome will be useful for further understanding of DNA structure-dependent transcriptional regulation.