

Z-DNA FORMING REGIONS IN THE HUMAN GENOME

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Introduction. Z-DNA is the left-handed helical structure of the usually right-handed B-DNA double helix structure. Z-DNA conformations have been found to cause mutagenesis and genetic instability [1]. In this study, human genome sequences potentially forming Z-DNA regions (ZDRs) were extracted and analysed for functional implications.

Materials and methods. Human genome sequence information was downloaded from UCSC Genome Browser and candidate ZDRs extracted using Perl scripts [2]. Only regions neighbouring transcription start (-1000 ~ +200 bp) and end (-200 ~ +1000 bp) sites were considered. Genes associated with candidate ZDRs were further analysed regarding gene ontology and potential binding of transcription factors.

Results and discussion. A total of 7,401 candidate ZDRs were detected of which 19.7% were associated with protein-coding genes on chromosomes (chr) 1, 2 and 17. GO analysis showed that among chr 1 candidate ZDRs transcription factors and genes associated with neuro developmental were over-represented (Table 1).

Table 1. GO over-representation of protein-coding genes associated with ZDRs on chr 1

Gene	GO accession/term	P-value
NFASC	GO:0007411 axon guidance	7.50E-05
TFAP2E	GO:0045944 positive regulation of transcription from RNA polymerase II promoter	3.90E-04
NGF	GO:0045664 regulation of neuron differentiation	4.31E-04
HES5	GO:0050767 regulation of neurogenesis	4.88E-04
HES5	GO:0006355 regulation of transcription, dNA-dependent	6.25E-04
FOXE3	GO:0006355 regulation of transcription, dNA-dependent	6.25E-04
TFAP2E	GO:0006355 regulation of transcription, dNA-dependent	6.25E-04
NGF	GO:0008284 positive regulation of cell proliferation	8.77E-04
PRKCZ	GO:0008284 positive regulation of cell proliferation	8.77E-04

Conclusions. Candidate ZDRs included previously reported ADAR1-binding regions and various promoter regions of transcription factors and miRNA genes that warrant an experimental follow-up to discern transcription regulation in response to Z-DNA formation and/or transcription factor binding.

References.

1. Wells R.D. (2007). Non-B DNA conformations, mutagenesis and disease. *Trends Biochem Sci.* 32(6):271-278.
2. Li H., Xiao J., Li J., Lu L., Feng S., Droge P. (2009). Human genomic Z-DNA segments probed by the Z alpha domain of ADAR1, *Nucleic Acids Res.* 37(8):2737-2746.