Symposium on Molecular Aspects of Cancer
Institute of Biotechnology
Ferdowsi University of Mashhad
December 20,2010

The discovery of possible regulatory regions inside the intron 2 of human *Bcl-2* gene

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BACKGROUND: Programmed cell death (PCD) plays an important role in a wide variety of physiological processes, such as removal of redundant cells during development, elimination of auto reactive lymphocytes, eradication of older and differentiated cells in most adult tissues and cancer. These processes are controlled via complicated processes by a variety of cis and trans acting regulatory elements (REs). Among these controllers, Bcl-2 family consists of a set of trans REs, which act as the major regulators of the PCD machinery, both positively (pro-apoptotic) and negatively (anti-apoptotic). The human *Bcl-2* (*hBcl-2*) gene is the first discovered member of Bcl-2 family, which acts as anti-apoptotic and its alterations contribute in numerous known diseases such as melanoma, lung carcinoma, schizophrenia and autoimmunity. Although various effects of hBcl-2 are discovered, the complications of its regulatory system have not been known yet. The *hBcl-2* gene is located at the long arm of chromosome 18, it spans over 196 kbp length and is consisted of 3 exons and 2 introns. The intron-2 (In-2) of this gene with 189322 bp length comprises 96% length of the gene, and it is believed that this gigantic size of the In-2 should not be superfluous. Finding critical regulatory regions and elements throughout the non-coding regions of the *hBcl-2* gene especially within In-2 might be useful to improve the existing strategies for the treatment of related diseases especially in cancer therapy. In present study, we used some *in silico* online biological methods to structure portray and identify likely regulatory regions with effectual elements such as transcription factor binding sites (TFBs), enhancer (ELEs) and promoter like elements (PLEs) which are distributed in the In-2.
RESULTS: According to our results, only about 27% of the length of the In-2 is composed of four classes of repetitive elements (REs) with noteworthy distribution patterns especially related to CR1s and L1s elements. However, our survey disclosed 956 TFBs on two strands of the In-2, consisting of 114 different TFBs (such as TW1, Gfi-1, AT-Alu, GAGA3-V1bR, HIF-1-Noxa and HIOMT-A-E4) with various distribution patterns and frequencies, which can bind to different transcription factors (TFs) and also with significant relationship to CpG islands, REs, PLEs and ELEs.
CONCLUSION: Overall, these results provide evidences to suggest that the conserved non-coding sequences in the In-2 of the *hBcl-2* gene are associated together with a particular pattern. Besides, we propose that some likely motifs for regulatory functions in the In-2, might be engaged in regulating the expression of this gene, which can be applied in molecular biology practices and cancer therapy.

Key words: Programmed cell death, Bcl-2 family, anti-apoptotic, intron, cancer therapy