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New Active Dioxin Response Element Sites in Regulatory Region of Human and Viral Genes

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Abstract : A computational search for dioxin response elements (DREs) in genes of proteins comprising the Ah receptor (AhR) cytosolic core complex was performed by highly efficient tool SITECON. Eventually, the following number of new DREs in 5'flanking region was detected by SITECON: one in AHR gene, five in XAP2, eight in HSP90AA1, and three in HSP90AB1 genes. Numerous DREs found in genes of AhR and AhR cytosolic complex members would shed a light on potential mechanisms of expression, the stoichiometry of unliganded AhR core complex, and its degradation vs biosynthesis dynamics resulted from treatment of target cells with the AhR most potent ligand, 2,3,7,8-TCDD. With human viruses, reduced susceptibility to TCDD of geneencoding HIV-1 P247 was justified by the only potential DRE determined in gag gene encoding HIV-1 P24 protein, whereas the regulatory region of CMV genes encoding IE gp/UL37 has five potent DRE, 1.65 kb/UL36 – six DRE, pp65 and pp71 – each has seven DRE, and pp150 – ten DRE. Also, from six to eight DRE were determined with SITECON in the regulatory region of HSV-1 IE genes encoding tegument proteins, UL36 and UL37, and of UL19 gene encoding bindingglycoprotein C (gC). So, TCDD in the low picomolar range may activate in human cells AhR: Arnt transcription pathway that triggers CMV and HSV-1 reactivation by binding to numerous promoter DRE within immediate-early (IE) genes UL37 and UL36, thus committing virus to the lytic cycle.

Keywords : dioxin response elements, Ah receptor, AhR: Arnt transcription pathway, human and viral genes
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