CHARACTERIZATION OF ELEMENTS THAT MODULATE GENE EXPRESSION IN CHINESE OVARY *HAMSTER* CELLS (CHO)

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The demand for biopharmaceuticals, as protein hormones, coagulation factors and antibodies is increasing, and the optimization of mammal expression vectors is necessary for productivity enhancement. In the present work we studied the effect of *cis* factors in the E1A cytomegalovirus promoter (CMV) in a luciferase-reporter gene expression vector (pGL4.14, Promega). Several CMV constructions were produced to analyze the effect of the presence of the hole and the truncated form of CMV E1A intron A (IA) and enhancer. It was also tested the presence of Z-DNA forming sequences cloned upstream the promoter with IA. All plasmid versions were transiently transfected in CHO-K1 cells. At least three independent experiments were performed for each construction. Our results showed a hundred-fold increase in the luciferase activity in the IA harboring constructions, comparing with the intronless version. Also, the deletion of 600 nucleotides downstream the IA did not affect the luciferase activity, although the removal of the 5' region of the CMV promoter reduced it in fifty percent. One of the Z-DNA sequences tested increased the luciferase activity significantly. Overall, it has been demonstrated that a minimal intron and the presence of Z-DNA inducers are able to enhance protein expression in CHO, suggesting their introduction in mammalian expression vectors.

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