An enhancer/promoter combination strengthens the expression of blood-coagulation factor VIII in non-viral expression vectors


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ABSTRACT. We explored the potential of fusion of hepatic locus control region 1 (HCR-1) with HCR-2 to express B-domain-deleted human factor VIII (FVIII) in four cell lines. B-domain-deleted human FVIII expression was controlled by HCR-1/HCR-2, followed by liver specific and ubiquitous promoters. Chimera enhancer HCR-1/HCR-2, followed by cytomegalovirus (CMV) promoter, gave 2-fold more FVIII expression in all cell lines (105.6 ± 2.8 for Hek-293, 68.8 ± 3.8 for HepG2, 34.8 ± 1.3 for CHO, and 27.2 ± 1.6 ng·mL⁻¹·10⁶ cells⁻¹ for L.N.) when compared to the vector with CMV alone (54.8 ± 3.3 for Hek-293, 32.4 ± 1.2 for HepG2, 18.6 ± 1.1 for CHO, and 10.1 ± 1.7 ng·mL⁻¹·10⁶ cells⁻¹ for L.N.). Elongation factor 1-α gene and human CMV promoters were more efficient than the promoters from the human α-1-antitrypsin gene, and fviil
was less efficient in hepatic cell lines. HCR-1/HCR-2, followed by strong promoters, increases FVIII expression \textit{in vitro}. Our results underscore the importance of cis sequences for enhancing \textit{in vitro} FVIII expression; this may be helpful for designing new strategies to improve heterologous expression systems.

\textbf{Key words:} Coagulation; Human factor VIII; Plasmid vector; Enhancer HCR-1 and HCR-2; Liver specific promoter; Mammalian cell lines