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Citation	The 2011 Hong Kong Inter-University Biochemistry Postgraduate Symposium, The University of Hong Kong, Hong Kong, 11 June 2011.
Issued Date	2011
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P-H041

Functional significance of the 3'-UTR in the mRNA of the stress-inducible protein CHOP/Gadd153

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How translation is regulated by the 3'-untranslated region (3'-UTR) of many messenger RNA is presently not fully understood. This issue is addressed in this study with regard to those mRNA species that are specifically expressed in stressed cells, as exemplified by the stress-inducible CHOP/Gadd153 mRNA. A human genomic fragment with DNA sequence corresponding to the entire 3'-UTR plus an additional 500bp immediately downstream from the polyadenylation site of CHOP/Gadd153 mRNA was cloned into the pEGFP-C1 plasmid. The transcription of this pEGFP-CHOP plasmid in HeLa cells produced two mRNA transcripts due to utilization of either the polyA-signal of the CHOP/Gadd153 gene or the pEGFP-C1 plasmid itself. The EGFP protein level in the pEGFP-CHOP transfected cells was several-fold lower than cells expressing the control (pEGFP-C1). The deletion of the first 171bp from the 5'-end of the 3'-UTR resulted in restoration of EGFP protein expression to a level comparable (and even slightly higher) to that produced by the control cells. In the presence of arsenite-induced cellular stress, a small increase in the EGFP protein expression level was observed in the pEGFP-CHOP transfected cells. However, the arsenite-induced increase in EGFP protein was greatly enhanced by at least twenty fold if the transcripts produced from pEGFP-CHOP also contained a 5'-UTR the same as that of CHOP/Gadd153 mRNA. Comparable mRNA levels were produced from these plasmids and were not affected by arsenite-stress. Our results suggest that the translation of CHOP/Gadd153 mRNA is dependent on stress signals mediated by the sequence context of its 3'-UTR.