Endoplasmic reticulum-directed recombinant mRNA displays subcellular localization equal to endogenous mRNA during transient expression in CHO cells

When expressing pharmaceutical recombinant proteins in mammalian cells, the protein is commonly directed through the secretory pathway, in a signal peptide-dependent manner, to acquire specific post-translational modifications and to facilitate secretion into the culture medium. One key premise for this is the direction of the mRNA encoding the recombinant protein to the surface of the endoplasmic reticulum (ER) for subsequent protein translocation into the secretory pathway. To evaluate the efficiency of this process in Chinese hamster ovary (CHO) cells, the subcellular localization of recombinant mRNA encoding the therapeutic proteins, erythropoietin (EPO) and Rituximab, was determined. The results show that ER-directed recombinant mRNAs exhibited an efficient recruitment to the ER when compared to an endogenous ER-directed mRNA, with no cytoplasmic translation of ER-directed recombinant proteins observed. These observations indicate that the recombinant mRNA, encoding ER-directed proteins, follows the same distribution pattern as endogenous mRNA directed towards the ER. Furthermore, the previous established fractionation method proves to be an efficient tool to study not only recombinant mRNA localization, but also recombinant protein trafficking between the ER and cytosol in CHO cells.

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