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Protein network reconstruction of CHO cell secretory pathway

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Introduction

Protein secretion is one of the major bottlenecks in the productivity of recombinant protein in mammalian cells. So far, there have been limited studies of the cell biology of the CHO cell and the potential of cell line engineering. To elucidate the poorly understood cellular processes that control and limit recombinant protein production and secretion, a system-wide study was initiated to identify possibly engineering targets relevant for therapeutic protein production.

Objective and Strategy

- Introduce a more systematic approach in improving the protein production in CHO cell lines
- Employ a guided approach that integrates protein function interaction network, gene expression and comparative studies of mouse and CHO cells.
- Identify functional gene targets within the secretory pathway for modification in order to increase protein production.

Pathway reconstruction

Proteins associated or linked to early secretion pathway were identified by manually curate available literature on mouse models and cell lines. The proteins found were used to identify CHO-K1 genes of the ERAD and protein folding pathway.

RNA-Seq transcriptome data

RNA was extracted with TRIzol reagent under different growth conditions and treatments from diverse sets of CHO cell lines.

Gene expression cluster analysis

A comparative expression analysis of CHO cells and mice allowed to evaluate CHO cell genes expression patterns and for identification of specific proteins and association with changed network arrangement in CHO cells.

Integrated gene expression network

The sub-network of genes associated with translocation and protein folding.

References