In vivo cleavage of solubility tags as a tool to enhance the levels of soluble recombinant proteins in *Escherichia coli*

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Abstract

Recombinant proteins are generally fused with solubility enhancer tags to improve target protein folding and solubility. However, the fusion protein strategy usually requires the use of expensive proteases to perform in vitro proteolysis and additional chromatography steps to obtain tag-free recombinant proteins. Expression systems based on intracellular processing of solubility tags in Escherichia coli, through co-expression of a site-specific protease, are useful for simplifying the recombinant protein purification process, for screening molecules that fail to remain soluble after tag removal, and to promote higher yields of soluble target protein. Herein, we review controlled intracellular processing (CIP) systems, tailored to produce soluble untagged proteins in E. coli. We discuss the different genetic systems available for intracellular protein processing regarding system design features, significant advantages and limitations of the various strategies.

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