A Non-chromatographic ELP-Intein Based Protein Purification System

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Inteins are self-splicing protein elements that can be engineered for different purposes, one of which is the development of self-cleaving purification tags. In previous work, we combined a pH-sensitive self-cleaving intein with a thermally-responsive elastin-like polypeptide (ELP), to create a very simple method for non-chromatographically purifying target proteins expressed in E. coli [1].

For complex human therapeutics protein productions, however, mammalian expression systems are typically required for more complicated post-translational processing ability. In this work, we demonstrate that ELP-tagged target proteins can be successfully secreted by Chinese Hamster Ovary (CHO) cells. Premature intein cleavage was observed as expected since the pH and temperature required for CHO expression is permissive for the cleaving reaction. Also, ELP was found to be genetically unstable after being integrated into the CHO genome.

Finding alternatives to solve the premature cleaving and ELP instability problem is the key goal of our current work. The strategies will be discussed, as well as the potential for the ELP-intein-based technique to provide a rapid, flexible, and inexpensive approach to purify CHO-expressed recombinant proteins.

[1] M.R. Banki, L. Feng, and D.W. Wood, *Nat Methods* 2, 659 (2005).